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VOLUME 31

1926

PUBLISHERS
AMERICAN MEDICAL ASSOCIATION
CHICAGO, ILL.

Medical
Wahr

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American Journal of Diseases of Children

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DRIED HUMAN MILK

V. ITS USE IN THE FEEDING OF PREMATURE INFANTS *

PAUL W. EMERSON, M.D.

AND

LAWRENCE W. SMITH, M.D.

BOSTON

In a previous communication, one of us [1] reported the preliminary studies of the use of dried breast milk as a food for infants. This work, which was begun in 1920, has been slowly progressing during the last five years. This paper is intended to supplement the earlier work by indicating its usefulness in special types of cases, and reports a number of premature babies who were fed this dried human milk in varying amounts and proportions, ranging from approximately the equivalent of half strength fresh breast milk to a concentrated form, somewhat in excess of the normal percentage values of fresh breast milk over varying periods of time from four days to five months. For purposes of convenience the cases will be grouped under two main headings, dependent chiefly on the method of production of the powdered milk. The first series represents a group of premature babies on the Boston Floating Hospital during the summer of 1924, who were fed on a preparation which was made with about from 35 to 40 pounds steam pressure. The second group were fed on a somewhat more satisfactory product made by improvement of the drying machine, so that only 15 pounds steam pressure was used, with a resultant much less marked diminution in the vitaminic content and an improvement in the appearance of the powder. This group was fed at the On-Shore Department of the hospital during the winter, over a much longer period of time and under conditions when more careful daily observations could be carried out. On this group, bacteriologic studies of the stools were made at frequent intervals, to study the intestinal flora as compared to that of stools from infants fed on fresh breast milk.

Several features of interest are noted from these studies. In the first place, as was indicated from the preliminary work, breast milk could be dried and utilized as a food for infants. With the original product, however, this was not entirely satisfactory in its clinical results,

* Received for publication, Sept. 26, 1925.

* From the Boston Floating Hospital.

1. Emerson, P. W.: Dried Human Milk: IV. Dried Human Milk as a Food for Infants, Am. J. Dis. Child. **30**:769 (Dec.) 1925.

as the infants seldom showed any gain in weight without the addition of protein in some form, usually calcium caseinate. They did, however, maintain their weight, and their condition in general was quite satisfactory otherwise. On this account, various improvements in the original method have been made. During the summer of 1924, the group of patients were fed on a powder obtained by drying the milk more rapidly than by the original method, but at a greater temperature. This group of cases, in general, likewise, failed to show any marked gain in weight without the addition of other food, especially in the form of protein. As noted previously, the second group was fed on a powder which was still further improved by drying for the same short time but at a considerably lower temperature. This group showed a steady but slow gain in weight. This was true over a long period of time, averaging eighty-seven days, during most of which no antiscorbutic or antirachitic food was given. In most instances, it will be noted from the history, abstracts and charts, that as soon as the baby received adequate caloric value in the formula, the gain in weight was comparatively satisfactory, but it was not always possible to supply this caloric need until a preliminary period of feeding had been given, during which the baby became adjusted to the food.

In all instances the infants took the food quite readily. Some of them occasionally regurgitated or vomited small amounts, but no more than would be expected with any premature infant even on fresh breast milk. If too strong a formula was given at the outset, then the stools tended to be rather frequent in number, even up to seven or eight per day. They were, however, usually very small and had the general consistency and appearance of the fresh breast milk stool, except that much of the bilirubin was converted to biliverdin.

It is a point of considerable interest and significance, we feel, that of this group of thirteen babies, fed on this food, only one premature baby, weighing 2½ pounds, died. This was due to an upper respiratory infection, and up to that time he had been doing satisfactorily on the formula. Eleven of these babies were definitely premature; one of them was probably premature, and only one of the group was definitely full-term and essentially a normal baby. Their weights varied at birth from 2¼ pounds up to 7⅛ pounds, all of the premature infants weighing under 5 pounds and five of them weighing less than 4 pounds. Five of the cases represent three twin pregnancies, the other twin in one instance having died at birth. Four of the cases represent three cases of eclampsia in the mothers, with one death. One infant (Case 4, Group 1) was a breech delivery with a prolonged four-day labor. Another infant (Case 3, Group 2) was born of a primiparous mother, aged 40. Another infant (Case 3, Group 1) had a suspicious history

of congenital syphilis but had a negative Wassermann test. Five of the mothers were from 16 to 18 years of age. Three of the babies were definitely illegitimate, and there is considerable question as to the legitimacy in two of the others. All of the Wassermann and Pirquet reactions were negative. Only two of the patients showed definite rickets on admission, namely, the premature twins, aged 2 months, of Italian parents.

GROUP ONE

The seven case histories in the first group are presented, and a table summarizing their important points follows. One of the babies was only on the formula for four days, and, accordingly, little information of value could be obtained. The other infants were on dried breast milk for a period of time ranging from twenty-one to seventy-seven days, and averaging forty-eight days.

REPORT OF CASES

CASE 1.—I. P., a girl, aged 4 weeks, was admitted July 8, 1924, and was discharged November 12. The diagnosis was prematurity. The feeding was regulated and the experimental feeding period lasted for seventy-two days.

Family History.—The father and mother and one older child were living and well; the baby was one of twins.

Past History.—The birth weight was 5 pounds; the infant was estimated to be one month premature, and was delivered normally. The mother had been ill and was not able to nurse either child.

Present Illness.—The child was admitted to the hospital because of failure to gain. She had been on a formula of whole lactic acid milk and Karo corn syrup and had vomited a good deal.

Examination.—This was essentially negative except for obvious under nutrition.

Progress.—On admission, the baby was put on 60 gm. of dried breast milk, giving a caloric value of 160 per kilogram of body weight. During the next twelve days she showed a gain in weight of 420 gm. At this time a control period of fresh breast milk was started, and during the next two weeks there was a further gain in weight of 160 gm. The formula was then shifted back to dried breast milk, and during the next seventeen days was slowly increased up to 75 gm. with a caloric value of about 190 per kilogram of body weight. On this there was a slight gain in weight of about 60 gm. Owing to the slight gain, fat-free cow's milk was added, with the view of raising the protein value of the food, and during a ten day period there was a gain in weight of 200 gm. On August 29, by the addition of calcium caseinate, a further increase in protein was made to 3.2 per cent. On this the baby developed slight diarrhea, and while there was an initial gain in weight of nearly 200 gm., there was a secondary loss of weight of about 120 gm. Accordingly, on September 17, a different brand of calcium caseinate was substituted for the brand used, with an immediate reduction in the number of stools. On September 21 a substitute feeding of dried reconstructed milk, developed at the Floating Hospital, was started, and during the course of the next few days the formula was shifted to 90 gm. of dried reconstructed milk. The child remained on this for a month, showing an increase in weight of approximately 600 gm. On October 24, the formula was changed to

dried cow's milk, one feeding at a time, until on November 1 she was entirely fed on dried reconstructed milk. After a trial period of about ten days, during which time there was a very marked gain in weight of about 600 gm., the infant was discharged home.

Remarks.—This subject was used similarly to that of the twin sister, in attempting to prove the value of dried breast milk as a substitute for fresh breast milk over a comparatively long period of time. This was followed by comparable periods on other dried forms of milk.

Case 2.—C. P., a girl, aged 2 weeks, was admitted July 8, 1924, and was discharged Jan. 1, 1925. The diagnosis was prematurity. The feeding was regulated and the experimental feeding period lasted for seventy-seven days.

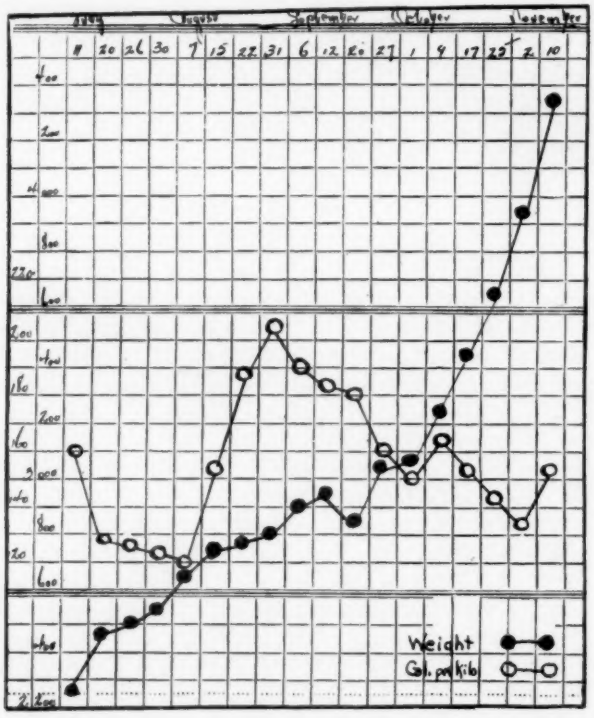

Chart 1.—A comparison of the gains in weight made on dried human milk, fresh human milk, and other forms of dried milk.

The family history, past history, present illness and examination were similar to those of Case 1.

Progress.—On admission, the infant was put on a fresh breast milk whey mixture for a week. This was then changed to whole breast milk. There was a satisfactory gain in weight of 420 gm. during this interval. On July 21, the child was put on dried breast milk in the same amount and strength. She remained on this until August 28, the amount being slowly increased from 60 to 80 gm. There was a steady gain in weight from 2,240 to 2,540 gm. On this date, approximately 1 per cent. of calcium caseinate was added to the formula, which three days later was changed to a different brand of calcium caseinate and increased to a total of 3 per cent. protein. She remained on this until September

17, when the calcium caseinate was omitted. On September 22, she was put on fresh breast milk in comparable amounts for a control period. In the month on fresh breast milk she gained 738 gm. Following this, a dried reconstructed milk formula was substituted slowly, having essentially the same formula. She remained on this until November 14, showing a further gain in weight of 510 gm. At this point, dried cow's milk was substituted as a further experimental study of the reaction to dried milk preparations. During a two-week period

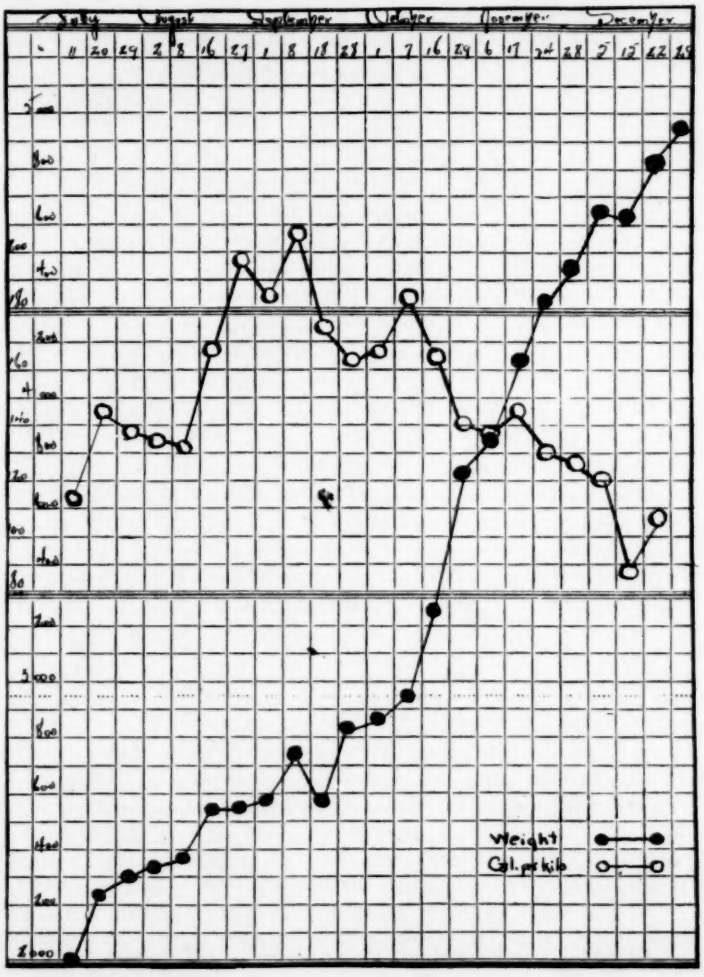

Chart 2.—The middle of the weight curve represents the gain made on fresh human milk, the first third on dried human milk, and the final third on dried reconstructed milk, and then on dried human milk.

on this formula there was a further gain of 676 gm. On December 9, the formula was changed to a simple whole milk solution in order to prepare the child for discharge from the hospital. Owing to family difficulties, she was not discharged for over three weeks, during which time she showed a further gain of 400 gm.

Remarks.—This patient was put on dried breast milk over a fairly long period of time, with the idea of comparing the rate of growth on this food to that on other dried milk preparations.

CASE 3.—K. T., a girl, aged 4½ months, was admitted July 9, 1924, and was discharged September 15. The diagnosis was prematurity and malnutrition. The experimental feeding period lasted for forty days.

Family History.—The father had a positive Wassermann reaction, but denied a history of syphilis. The mother's Wassermann reaction was negative. There was one older, somewhat underweight, child living and well. The mother had two miscarriages before the birth of the present child, at two and three months pregnancy, respectively.

Past History.—The baby was thought to be a scant 7 months premature infant, delivered normally, with a birth weight of 4½ pounds. She was breast fed for six weeks and then put on a whole milk formula.

Present Illness.—The infant was admitted to this hospital because of failure to gain. She weighed 4 pounds (1,840 gm.) on admission.

Examination.—The baby showed no particular physical abnormalities, other than her extreme small size and emaciation. The liver was felt 4 cm. below the costal margin, the spleen was not palpable. The lymph nodes generally were enlarged slightly. There were some scars on the perineum suggesting healed condylomas.

Laboratory Findings.—The Wassermann and Pirquet tests were negative. The urine and stool examinations were negative. There was a slight secondary anemia, with a red cell count of 3,872,000 and a white cell count of 5,320.

Progress.—On admission, the child was put on a whole milk formula, and gained 100 gm. during a week. She was then placed on dried breast milk for a period of forty days, during which she just held her weight, although there had been several times when there was a gain of from 50 to 60 gm. She was then put onto fresh breast milk for four days, on which she developed diarrhea and vomited. For the ten days before discharge she was again put on a whole milk formula in order to permit her transfer to another hospital.

Remarks.—This case seemed to be rather unusual, with a question of a syphilitic background. During the infant's entire stay in the hospital she ran a somewhat subnormal temperature, and required practically the same care as a premature infant. It is interesting to note that she maintained her weight and nutrition on the dried breast milk, took the feedings well and had no vomoting or diarrhea.

Subsequent History.—This patient throve well on gradually increasing strength cow's milk formulas until the following spring, when she was admitted to the Boston dispensary with acute volvulus, of which she died.

CASE 4.—J. B., a boy, aged 5 weeks, was admitted July 23, 1924, and was discharged October 1. The diagnosis was prematurity. The feeding was regulated and the experimental feeding period lasted for fifty-eight days.

Family History.—The mother, father and two other children were living and well. There was one miscarriage five years prior to the birth of this infant. One child died of jaundice at the age of 2 weeks.

Past History.—The patient was a full term baby, delivered by breech extraction after prolonged labor lasting for four days. He was supposed to have been a "blue baby." He was breast fed for two weeks and then put on the bottle.

Present Illness.—The infant was admitted with a history of vomiting and loss of weight for three weeks prior to admission.

Examination.—A poorly developed and poorly nourished boy, with omphalitis, seborrheic dermatitis of the scalp and a small umbilical hernia was seen.

Progress.—The infant was put on full strength dried breast milk (75 gm. to 720 c.c. of water). On this he developed marked diarrhea, with from 6 to 8 stools daily. He was changed by mistake to fat free lactic acid milk for twenty-four hours, but was then put on a low dilution of dried breast milk (25 gm. to 600 c.c. of water). During the next six weeks, this was increased slowly 5 gm. every two days up to 75 gm. On this the stools were from 1 to 2 daily, and he maintained his weight after an initial loss of 200 gm. He then began to gain slowly. On admission, his weight was 2,680 gm., which fell to 2,480 gm. with the diarrhea. On August 25, his weight was 2,800 gm. On August 29, 0.25 per cent. calcium caseinate was added and again on September 2 a further 0.25 per cent. was added, raising the percentage to 2. On this he showed a further gain in weight of just 200 gm. From September 7 to 17 he remained on this

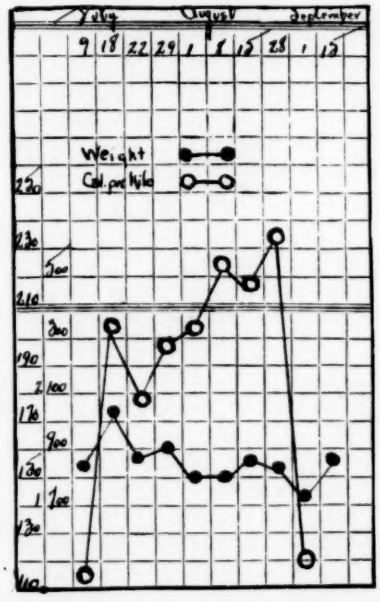

Chart 3.—The weight curve of an emaciated premature infant, weighing 4½ pounds, fed on dried human milk for forty days.

formula except for two days (September 7 and 9), when the supply of dried breast milk was inadequate and he had to receive some cow's milk in addition. On September 18, he was shifted to a dried cow's milk formula in preparation for discharge, which because of diarrhea was changed over to cow's milk, half and half, on which he was discharged.

Remarks.—This patient was on dried breast milk for sixty days. This treatment represented an attempt to utilize dried breast milk when fresh breast milk would normally have been indicated, namely, in a malnourished premature baby. After an initial loss in weight of 200 gm., the result of overfeeding and lack of necessary time for adjustment to this food, the child began to gain slowly, and from the low weight of 2,480 gm. his weight rose to 2,860 gm., a total of approximately 400 gm.

Case 5.—M. M., a boy, aged 1 month, was admitted July 28, 1924, and discharged July 31. The diagnosis was ophthalmia neonatorum. The experimental feeding period was for four days.

Family History.—There was a bad family history, with considerable question as to the legitimacy of this child. The mother, aged 32, had seven children living and well. She had had one miscarriage. The father had tuberculosis and epilepsy. An aunt, aged 16 years, had syphilis.

Present History.—The infant weighed 5½ pounds at birth. The mother thought the baby was about 1 month premature. He was cared for by the syphilitic aunt during the first two weeks, and he had a discharge from both eyes since birth. He was breast fed for two days, then fed on malted milk according to the directions on the bottle. For the last three days before admittance, the child had about eight stools daily.

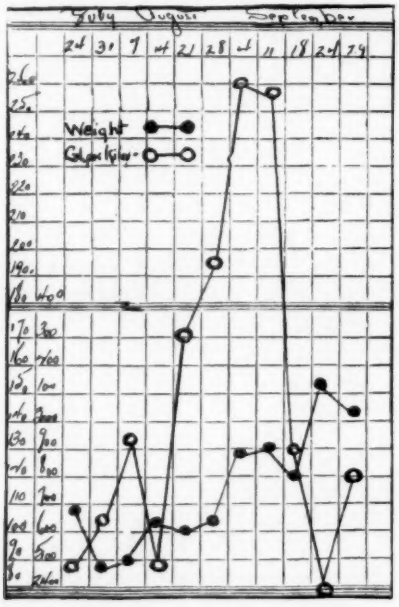

Chart 4.—The weight curve of a malnourished premature baby who ordinarily would have been fed on whole human milk. Fed here on dried human milk.

Examination.—A malnourished, premature appearing infant with a bilateral atypical ophthalmia neonatorum, and badly excoriated buttocks was seen.

Progress.—As the infant was premature, he was put on half strength dried breast milk (25 gm.). After four days he was discharged to the Eye and Ear Infirmary because of the ophthalmia. During this period he took the food well. there was no vomiting and the stools were normal in appearance. He maintained his weight during these four days.

Case 6.—A. L., a girl, aged 2 months, was admitted August 21, and discharged December 11. The diagnosis was prematurity. The feeding was regulated and the experimental feeding period lasted for twenty-three days.

Family History.—The father, aged 34, was living and well. The mother, aged 18, showed a marked case of hyperthyroidism and developed acute

toxemia, so that the baby, one of twins, was delivered prematurely at seven months.

Present History.—The birth weight was 2½ pounds; that of the twin was 2¼ pounds. Both babies had marked icterus, which persisted for several weeks.

Present Illness.—The baby was admitted to the hospital because of a history of vomiting for three days prior to admission.

Examination.—There was marked rickets with craniotabes, a rosary and epiphyseal enlargement. There was considerable lymph node hyperplasia and a moderate seborrheic eczema of the scalp. Aside from the rickets, the chief findings were loss of weight and malnutrition.

Progress.—On admission, the baby was put at once onto half strength dried breast milk, with fat-free cow's milk added to increase the protein percentage to 3 per cent. The admission weight was 2,005 gm. She was kept on dried breast milk in combination with added proteins for twenty-three days, during which time she

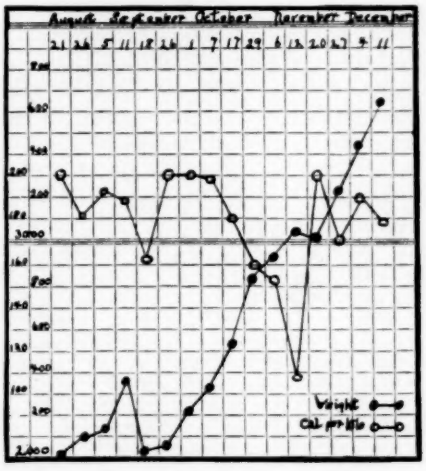

Chart 5.—Weight curve of a premature baby fed on dried human milk, fresh human milk, and finally on other forms of dried milk.

gained 120 gm. Following this experimental period, she was put on fresh breast milk for a control period of two weeks, during which time her weight increased 400 gm. At that time the formula was changed to dried reconstructed milk of the same percentage. During a period of twelve days there was a further gain of 170 gm. At that time 1 per cent. of protein was added in the form of calcium caseinate. There was a gain in weight of 280 gm., but marked diarrhea developed and the formula had to be reduced with omission of the calcium caseinate. During the next three weeks, she was on an albumin milk formula, the sugar percentage being slowly increased up to 6 per cent. On November 24, in anticipation of discharge, the infant was put on a simple half and half dilution of lactic acid milk and dextrimaltose.

During the experimental breast milk feeding period she received no cod liver oil or orange juice. These were begun on September 18, after the control period with fresh breast milk was begun.

Remarks.—This case illustrates again the fact that dried breast milk can be utilized as a substitute for fresh breast milk in premature infants.

CASE 7.—E. L., a girl, aged 2 months, was admitted August 24, and discharged December 27. The diagnosis was prematurity. The feeding was regulated and the experimental feeding period lasted for twenty-one days.

The family history, past history, present illness and examination were the same as those of Case 6, except that this patient had developed marked diarrhea, with from twenty to thirty watery stools for three days.

Progress.—On admission, the infant was put on half strength dried breast milk, with added fat-free cow's milk. The admission weight was 1,960 gm. This was gradually increased in strength to three-quarters the percentage value of whole breast milk. Five days after admission calcium caseinate was added, increasing the protein percentage to 2.3 per cent. The child remained on this formula for three weeks, during which time she showed a gain in weight of 140 gm. On September 22, a control period of three weeks on whole strength fresh breast milk was started. A further gain in weight of 196 gm. resulted. On October 10, she was transferred to a formula of dried reconstructed milk, having the percentage value of 3.3 per cent. fat, 7 per cent. carbohydrates, and 1.5 per cent. protein, and a caloric value of 200 per kilogram. One per cent. of calcium caseinate was added on October 23, which was continued for ten days, during which time there was a marked gain in weight of 230 gm. She was then put on dried cow's milk, but developed acute diarrhea and was put on fresh breast milk for a period of ten days, then gradually shifted to a formula of lactic acid milk and Karo corn syrup, on which she was discharged home, with a weight of 3,444 gm.

During the experimental period, no cod liver oil or orange juice were given. The infant took the dried breast milk well without vomiting or diarrhea. She had such marked rickets that in addition to the cod liver oil she was given ultraviolet treatment at the On-Shore Department, beginning December 11.

TABLE 1.—*Summary of Results in Group 1*

Case	Period in Days on Dried Breast Milk	Gain in Weight During Experimental Feeding Period, Gm.	Age on Admission	Weight on Admission, Gm.	Total Amount Dried Breast Milk, Gm.	Average Calories per Kg. of Body Weight	Average Number of Stools	Vomiting
1	72	402	2 wk.	2,060	4,265	180	2-4	Rarely
2	77	529	2 wk.	1,800	4,425	180	2-3	None
3	40	80	4½ mo.	1,840	2,620	200	2-3	None
4	58	608	5 wk.	2,680	3,637	160	1-4	Rarely
5	4	...	1 mo.	2,360	120	75	2-6	None
6	23	120	2 mo.	2,005	1,600	200	3-5	Rarely
7	21	80	2 mo.	1,960	1,365	180	2-3	Rarely

GROUP TWO

The six case histories in this second group are presented, along with a table summarizing their important points. These infants were fed over a period of time ranging from twenty-six to 137 days, three of them being fed on this product over 120 days and the whole group averaging eighty-seven days.

CASE 1.—J. S., a boy, aged 4 weeks, was admitted Dec. 25, 1925, and was discharged May 25, 1926. The diagnosis was malnutrition. The experimental feeding period was for 137 days.

Family History.—The parents were both living and well. The child was probably illegitimate.

Past History.—The infant was probably born at full term, born spontaneously without medical attention. He was breast fed for one week, and then put on the bottle because of a postpartum septicemia of the mother.

Present Illness.—The baby was admitted because of loss of weight and marked constipation. His temperature on admission was just under 93 F., the result of exposure in extremely cold weather.

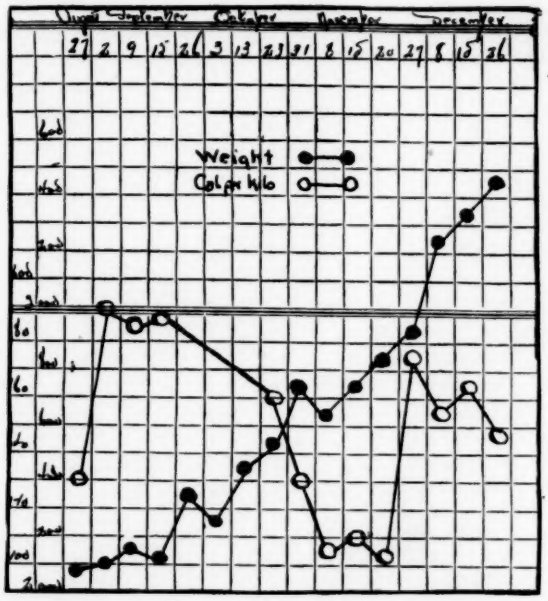

Chart 6.—Weight curve of a premature baby fed on dried human milk, on fresh human milk, and then on lactic acid milk with Karo.

Present Examination.—The physical examination was entirely negative, except for the characteristic old-man facies and wrinkled skin associated with marked malnutrition.

Progress.—On admission, the infant was put on two-third strength dried breast milk with a caloric value of about 125 per kilogram of body weight. This was increased to three-fourths strength, giving a caloric value of 145 kilogram of body weight. On this formula there was some tendency to loose stools. The infant took it well, however, and there was no vomiting. He was changed to fresh breast milk for four days with no marked decrease in the number of stools, and accordingly was put back on full strength dried breast milk. He remained on this from December 27 to May 5. The amount was slowly increased from 720 c.c. to 1,050 c.c. There was a gain in weight of 1,078 gm. The weight curve flattened out somewhat during the next three months, and although still climbing slowly showed very little change during the fourth. At

that point, orange juice in amounts equivalent to 8 c.c. per kilogram of body weight was begun. The gain in weight after this was somewhat more rapid. On April 9, cod liver oil also was added, and, during the course of the next month, 300 gm. increase in weight was noted. He was then gradually shifted to dried cow's milk, on which he was discharged home, showing a further gain in weight of 600 gm. during the next three weeks.

Remarks.—This case represents one in which the prolonged use of dried breast milk over several months was studied. The baby was malnourished on admission, but in other respects he was normal. There was a steady gain in weight over the entire experimental feeding period of five months, this tending, however, to slow up after from two to three months, probably due to some

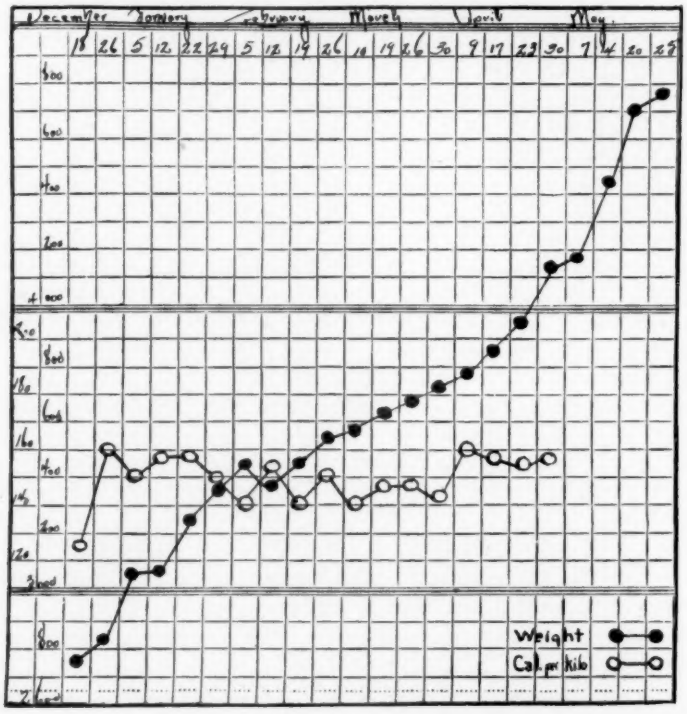

Chart 7.—Weight curve of a premature baby fed on dried human milk for 137 days, with orange juice and cod liver oil added after three months.

deficiency in the vitaminic content of the food, for, by adding vitamins in the form of orange juice and cod liver oil, the rate of growth was again increased to normal.

CASE 2.—J. G., a boy, aged 2 days, was admitted Jan. 5, 1925, and was discharged May 27. The diagnosis was that the baby was normal. The experimental feeding period lasted for 124 days.

Family History.—Unknown. An illegitimate baby, who was referred to us through one of the charitable orphan asylums.

Past History.—The infant was supposedly born at full term, normally delivered, with a birth weight of 7 pounds, 2 ounces. He was never breast fed, but was put on a formula of two-fifths cow's milk.

Examination.—The infant appeared to be normal, with a rather marked icterus neonatorum.

Progress.—The baby was put on two-thirds strength dried breast milk (50 gm.) on admission. During the course of a week he showed a tendency toward a rather large number of stools (from 7 to 9 a day), and occasionally he spit up from 10 to 30 c.c. of food. After one week, the formula was reduced by one half in an attempt to cut down the number of stools. No improvement was noted after a week and there was a further loss of weight. Accordingly the formula was changed to fresh breast milk of the same dilution. The stools remained high in number, from five to seven, and, after a week, it was decided that the results were just as satisfactory with the dried milk, and accordingly the baby was put back onto a three-fourths strength formula, containing 45 gm. During the next ten days there was a gain in weight of 57 gm. The formula was then increased to seven-eighths strength, and after ten days was further increased to full strength. On February 14 the amount was increased by the addition of 12 gm., and four days later it was again increased to 84 gm. of powdered milk in 840 c.c. of water.

During the two month period following the initial loss in weight of 300 gm., there was a subsequent gain of 300 gm. with an additional 250 gm. During the next month the infant remained on the same formula, except that occasionally when he was particularly hungry he would be allowed an additional ounce of formula. The stools averaged from one to three a day. No vomiting occurred. During these two months there was a further gain of 600 gm. Orange juice was started on March 17, and cod liver oil (10 minims) on April 9, which was increased to 20 and 30 minims on subsequent weeks. On May 6, an experimental period of one week was started, during which time dried fat-free breast milk was added to increase the protein value of the food, and a very striking gain in weight of 300 gm. during this period resulted. Gradually, beginning May 14, dried cow's milk feedings were substituted and the infant was discharged on May 27 weighing 4,989 gm., his initial weight being 2,948.

Remarks.—This case represented an attempt to demonstrate the value of dried breast milk as compared with fresh breast milk in feeding a normal infant, and, after a five month experimental feeding period, it semed safe to say that the two foods are to all intents and purposes comparable, if vitamins are added to replace the amount lost by drying.

CASE 3.—H. M., a boy, aged 3 weeks, was admitted Jan. 6, 1925, and was discharged May 27. The diagnosis was prematurity. The feeding was regulated, and the experimental feeding period lasted for 130 days.

Family History.—The mother, aged 40, was living and well. Nothing was known of the father.

Past History.—This infant, a boy, was illegitimate (?), born by cesarean section at 7 months. The mother was a primipara, with beginning symptoms of eclampsia. The infant was one of twins, weighing 4 pounds 6 ounces at birth. The twin weighed 2½ pounds and died four days later. The mother had little or no milk, and the baby had been on a half and half whole cow's milk formula for ten days, with a loss of about 8 ounces.

Examination.—This was negative except for evidence of prematurity and malnutrition.

Progress.—The baby was put on half strength dried breast milk (25 gm.). This was increased 5 gm. at a time every few days up to full strength (60 gm.). On this formula the infant showed a slow but steady gain in weight, which was only very slight at first, because of his low caloric intake. The stools showed some tendency to be loose and the child occasionally regurgitated a few cubic centimeters. Subsequently, the formula was increased in amount to 72 gm., and 10 days later was again increased to 80 gm. On this there was a further steady but slow gain in weight. After eleven weeks, orange juice was added (8 c.c. per kilogram of body weight.) Two weeks later 10 minims of cod liver oil was given, increasing this by 10 minims one and two weeks later. On May 6, the

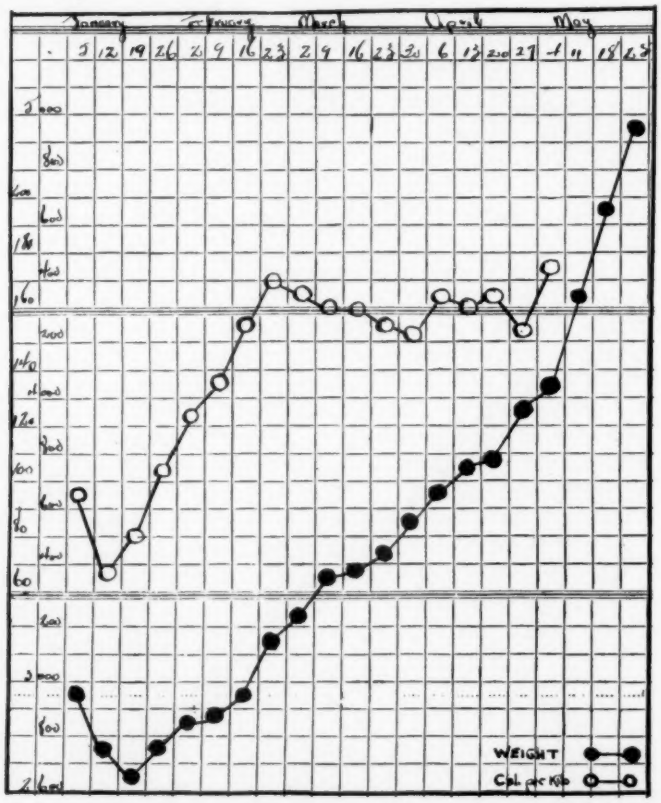

Chart 8.—Note the sharp rise in weight, May 6, when additional protein was added to dried human milk, in the form of dried skimmed human milk.

strength of the formula was increased by the addition of an equivalent amount of dried skim breast milk. During the course of one week, the infant showed a gain of 284 gm. He was then slowly changed to dried cow's milk prior to discharge home. On admission, he weighed 1,786 gm., and at the end of 130 days on dried breast milk he had gained 1,332 gm.

Remarks.—This case represents one in which the prolonged use of dried breast milk without added vitamin showed a satisfactorily steady gain in weight. As in the case of fresh breast milk, a more rapid gain was noticed by the

addition of protein, in this instance in the form of dried skimmed breast milk. It illustrates particularly well the value of such a product as a satisfactory substitute for fresh breast milk.

CASE 4.—H. T., a boy, aged 3 weeks, was admitted Jan. 14, 1925, and was discharged March 26. The diagnosis was prematurity and bronchial pneumonia. The feeding was regulated and the experimental feeding period lasted for sixty-five days.

Family History.—The father and mother were living and well. Both parents were young, each being under 20 years.

Past History.—The baby was 2 months premature for no recognizable reason. His birth weight was 3 pounds, 3½ ounces. On admission, he weighed 2 pounds, 8 ounces. The infant had been on a one-third whole milk formula, as the mother had no breast milk. The temperature had been subnormal since birth.

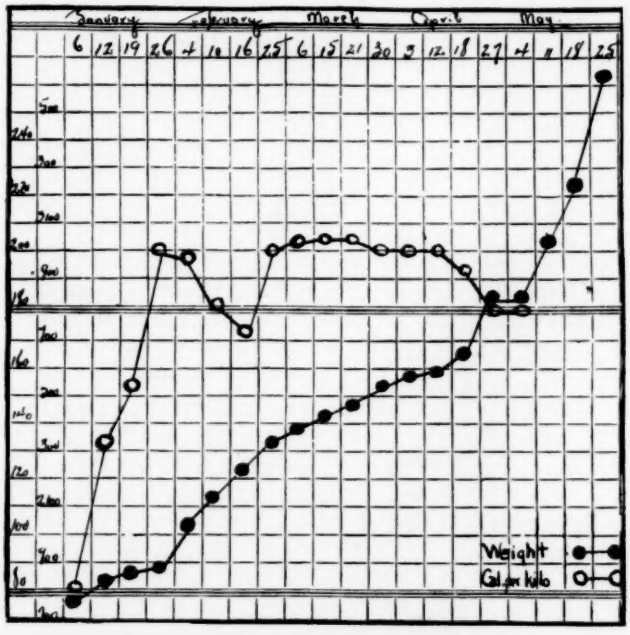

Chart 9.—Orange juice added after eleven weeks to dried human milk, cod liver oil after thirteen weeks. Dried human skimmed milk added May 6.

Examination.—The physical examination was negative, except for the diminutive size and obvious malnutrition of the infant.

Progress.—On admission, the infant was put on half strength dried breast milk (18 gm.), having a caloric value of 100 per kilogram of body weight. The formula was slowly increased by the addition of a few grams at a time up to full strength breast milk (36 gm.). On this, over a period of 2 months, the child held his weight and showed a slight gain of 170 gm. At that time, he was receiving about 200 calories per kilogram. The stools were increased in number, and he had been spitting up for two or three days, so the formula was reduced to half strength again. On this he seemed to improve but showed a slight loss of 30 gm. in weight. The formula was increased by the addition of dried fat-free breast milk on March 19, and a gain in weight of 45 gm. was

noticed during the next six days. On March 21, there was a rise in temperature accompanied by marked vomiting. The infant was put on fresh breast milk, but no improvement was noted, and during the course of the next three days he became more and more feeble, dying apparently of an upper respiratory infection.

Remarks.—This was an interesting case, as the patient was the smallest baby to be fed with dried milk. It was satisfactory to note that he held the weight, even gained slightly and appeared to be doing fairly well until infection supervened.

CASE 5.—J. H., a boy, aged 11 days, was admitted April 3, 1925, and was discharged May 26. The diagnosis was prematurity. The feeding was regulated and the experimental feeding period lasted for forty-one days.

Family History.—The premature delivery was due to eclamptic toxemia in a primiparous mother, aged 16, who subsequently died. The mother had always been well previously. The child was illegitimate and nothing was known of the father.

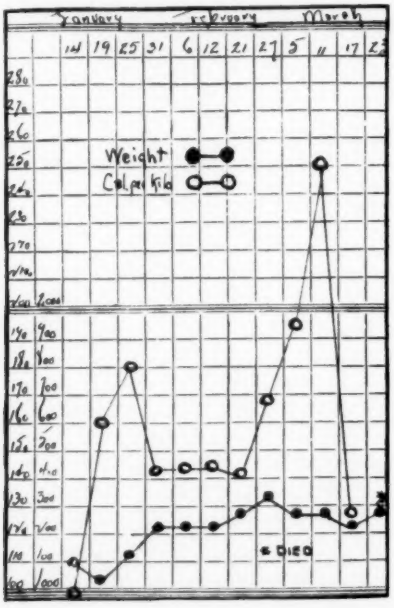

Chart 10.—A slight gain in two months of a premature baby fed on dried human milk.

Past History.—The infant weighed 3 pounds and 14 ounces at birth, and was on a diluted breast milk formula during the eleven days preceding admission to this hospital.

Examination.—This was negative except for prematurity and resultant malnutrition.

Progress.—The baby was put on a formula of half strength dried breast milk (18 gm.), giving a caloric value of 80 per kilogram of body weight. On this formula the stools were normal. After a week the protein percentage was increased by the addition of dried fat-free breast milk, and again on April 13 and 21, fat-free dried breast milk was added until the protein value was 1.5 per cent. with the fat remaining at 1.75 per cent. On this there was a more rapid gain in weight. On April 27, the amount of the formula was increased. On May 9, the

formula was increased by an additional 5 gm. of dried whole breast milk, and a further gain in weight was noted during the next week. Beginning May 14, the baby was slowly changed to a lactic acid Karo formula in order to prepare for his discharge. The experimental feeding period was, accordingly, forty-one days. During this period there was a gain in weight of 525 gm. This baby always vomited or spat up, which continued after the change of formula to lactic acid.

Remarks.—This case represented another premature infant who was fed in this instance a low caloric formula of dried breast milk, keeping the fat under 2 per cent. Even on this low formula, there was a satisfactory gain in weight over the experimental period. This case may be constrasted with Case 3, in which the infant received a relatively high caloric value and full strength breast milk during practically the entire experimental feeding period.

CASE 6.—E. C., a boy, aged 3 days, was admitted April 8, and was discharged May 27. The diagnosis was prematurity. The feeding was regulated.

Family History.—The mother, aged 28, was living and fairly well. She worked in a shoe factory. The father was living and well as far as is known.

Past History.—The baby was born spontaneously at home without medical attention. It was estimated as a 7 months, premature infant, weighing 1,870 gm. The mother welcomed the opportunity to have hospital care for the baby, as she had no breast milk.

Examination.—The baby was small and extremely weak. There was marked icterus, but no other abnormalities were noted.

Progress.—On admission, the infant was put on half strength dried breast milk. He had to be fed by gavage for practically the entire stay in the hospital, as he remained too weak to use even a Breck feeder well. The formula was slowly increased by the addition of dried fat-free breast milk, raising the protein to 1.2 per cent. On May 4, after a month on the formula with a gain in weight of only 60 gm., the infant was transferred to a control period of fresh breast milk, on which he began immediately to gain rapidly. Beginning May 8, it was slowly shifted one feeding at a time to a Karo-lactic acid formula on which he was discharged.

Remarks.—This case is typical of the results obtained by this method of feeding. Very small premature babies will take the dried breast milk well without vomiting and without diarrhea. They will hold their weight and show a slow gain over a comparatively long period of time, but do not, as a rule, show as comparable a gain as on fresh breast milk. This suggests an inherent fault in the method of production rather than in the milk itself.

TABLE 2.—*Summary of Results in Group 2*

Case	Period in Days on Dried Breast Milk	Gain in Weight During Experimental Feeding Period, Gm.	Age on Admission	Weight on Admission, Gm.	Total Amount Dried Breast Milk, Gm.	Average Calories per Kg. of Body Weight	Average Number of Stools	Vomiting
1	137	1,786	4 weeks	2,636	12,939 W 175 FF	150	3	None
2	124	1,616	2 days	2,806	10,836 W 175 FF	150	3	Rarely
3	130	1,332	3 weeks	1,786	9,334 W 175 FF	150	3	Occasional
4	65	184	3 weeks	1,105	1,636 W 376 FF	150	3	None except terminally
5	41	525	11 days	1,530	1,067 W 858 FF	150	3	Small amts. occasionally
6	26	60	3 days	1,870	624 W	100	3	Regurgitated occasional small amts.

COMMENT

These cases seem to represent a step forward in infant feeding. The hospital is rather proud of the record which it has had during the last two years of losing only one premature baby, and feels that this result is largely due to the use of breast milk. Through the Social Service Department, it has been the custom of the hospital for many years to secure breast milk for the sickest patients and the premature babies.

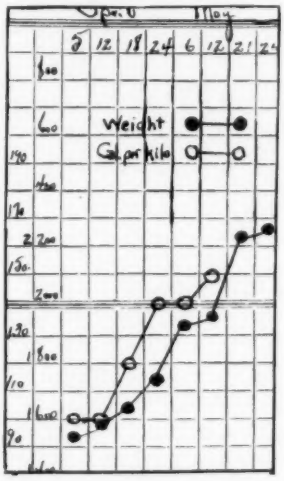

Chart 11.—Weight curve of a premature baby fed on dried human milk with a low fat, and high protein content.

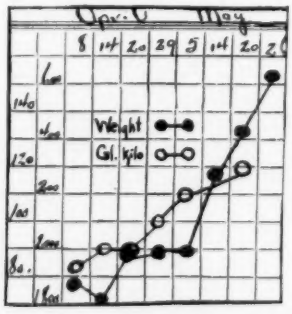

Chart 12.—Sharp rise in weight curve when a premature baby was fed on fresh human milk after dried human milk.

Often this has been insufficient to meet our needs, and the original purpose of attempting during the winter to preserve breast milk for utilization during the summer months on the Hospital Ship now has become an actuality. The organization which has been in force during the summer months is now continuing the work of collecting breast milk during the winter months. This is dried on the experimental machine previously

described.[2] In this way we are able to have a sufficient quantity of breast milk available at all times for use when indicated. Thus far, the work has been conducted on an experimental basis, but it has now reached the stage when we feel that it is ready for presentation to the profession, with the hope that others will make use of this work and benefit by our experience and mistakes.

As will be noted on careful study, the cases bring out several striking features. In the first place, the babies like the food. They take it well. There is rarely any vomiting of pathologic significance. Usually there is none or at most only the regurgitation of a teaspoonful or so of the formula, such as we see in most small babies. In the second place, it is handled readily by the digestive tract of the baby and the stools are usually of the general consistency, odor, and bacterial content as those of infants on fresh breast milk. They differ only in tending to be more green, due probably to partial oxidation of the bilirubin. In the third place, even on the original product, fortified by small amounts of carbohydrate and which left much to be desired, the babies maintained their weight, and now with only relatively slight changes in the methods of production of the powdered milk, we are able to procure a steady gain in weight. This is not as marked a gain, however, as is ordinarily found by using fresh breast milk, and we feel that we still unquestionably can improve the technic of drying so that comparable results should be obtained with those of the fresh milk.

One of the most interesting facts which these studies emphasize is that breast milk, either in its natural or dried form, is not a perfect food for all babies and that it is necessary often to add to the protein value in order to secure growth. This may have some theoretic consideration of importance. It seems strange that human milk should have so low a protein percentage as compared to the milk of other mammals, for prematurity seems to be a much more common thing in man. A premature infant is deficient not only in weight but particularly in certain of the stored dietary factors, notably iron in the liver. Even under the most careful dietary supervision, it is well recognized that a form of rickets is almost sure to result in babies, especially twins, who are 2 months, or more, premature. Such premature infants apparently need a relatively large amount of protein in order to grow normally, and our work confirms the expressed opinion of many other pediatricians of this fact. All of the infants, even in the earlier group, showed a very much more rapid gain in weight following the increased protein value of the formula by the addition of the various forms of precipitated casein, obtained from cow's milk. It seems more logical from our stand-

2. Emerson, P. W., and Smith, L. W.: Notes on the Experimental Production of Dried Breast Milk, Boston M. & S. J. **191**:20 (Nov. 13) 1924.

point to supply the necessary additional proteins in the form of breast milk protein, and in certain of these infants it will be noted that they show the same if not greater gains in weight over comparatively short periods of time by the addition of skimmed breast milk in powdered form.

Furthermore, the use of skimmed dried breast milk seems to offer a very logical food in cases of intestinal intoxication associated with marked fermentative or infectious diarrheas, and it is particularly that phase of the work which we are studying this year. In this way, a formula high in carbohydrates and protein, similar to the fat free, cow's milk formulas commonly in use, can be obtained. In the series of premature babies cited in the foregoing, many of the infants were unable to handle the full fat content of whole breast milk, and by the addition of this skimmed breast milk a diluted formula could be fortified to a 2 or 3 per cent. protein successfully, which was much more readily tolerated by these babies. This supplied the necessary protein requirements for growth without producing digestive disturbances as the result of too high a fat content.

It will be noted also in the history abstracts that the use of powdered breast milk was compared in the same baby to other dried milk preparations made from cow's milk, with very favorable results. It is reasonable to suppose that by drying breast milk, the casein curd is made even finer and rendered more soluble than in its fresh state, just as it is in the other forms of dried cow's milk, and on theoretic grounds should be even more readily handled than the fresh milk.

It has been demonstrated that even whole breast milk can be dried and kept without serious alteration for a period as long as five years. A considerable amount of the milk used in the experimental feeding was at least from eight to ten months old. The babies took this product just as well, and gained just as much as on milk dried the day before it was used. Occasional periods would be encountered when all the babies in the ward would have an increased number of stools and would spit up small amounts of food. This, apparently, was due to variation in the milk rather than to the method of production, as similar upsets of a trivial character may be noted in normal breast fed babies, due, usually, to indiscretions in the mother's diet or to irregularities in her health.

The charts and tables are self-explanatory, and illustrate the points before mentioned. They emphasize the fact which we are trying to bring out, that dried breast milk is the nearest approach to a logical substitute for fresh breast milk which can be found; that by drying any surplus milk which can be secured, we have a method available for the preservation of the milk and a product which can be kept apparently quite indefinitely, until it is needed for some premature infant whose

mother's supply gives out, or for some acutely sick baby in whose condition nothing but breast milk is indicated. It possesses the further advantage of being available at a distance for infants too sick to bring to the hospital and too far away for the fresh milk to be transported to them.

SUMMARY AND CONCLUSIONS

A series of thirteen cases is presented, in which the infants were fed dried breast milk over periods of time ranging from four to 137 days. Eleven of these were premature infants, weighing under 5 pounds, one was probably premature and one was a normal new-born baby used as a control.

The cases are divided into two groups, based on a slight modification in the technic of production. The first group was fed on milk dried at a higher temperature. The average feeding period was forty-eight days, as compared to the second group which averaged eighty-seven days. The second group was fed for a longer period of time and on powder prepared at a much lower temperature.

In both groups there was a slow but steady gain in weight, which was more marked, however, in the latter group. The addition of protein to the formula either in the form of dried fat-free breast milk or casein resulted in a more rapid gain in weight.

The experimental evidence seems to prove that dried breast milk can be utilized as a substitute for fresh breast milk, and that it is particularly indicated in premature infants and in those with severe intestinal intoxications, in whom fresh breast milk is ordinarily indicated but is not available.

The results of these experiments lead us to believe that by very slight further modification in the method of drying, a still better product can be obtained which would be available at all times for indicated cases.

BACTERIOLOGIC STUDIES OF THE RESPIRATORY PASSAGES

VI. HEMOLYTIC STREPTOCOCCI IN THE PHARYNX AND TONSILS OF INFANTS AND CHILDREN *

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AND
I. HARRISON TUMPEER, M.D.
CHICAGO

The importance of hemolytic streptococci as the cause of fatal infections in infants and children is generally recognized. In bronchopneumonia, empyema, otitis media and in other serious conditions, these organisms are the predominant bacterial agents. In a previous study [1] it was pointed out that these streptococci are commonly found in normal and diseased conditions of the upper respiratory tract. These organisms were recovered from swab cultures of the pharynx and tonsillar surfaces in 61 per cent. of children, aged from 6 to 15 years, with simple hyperplastic tonsils. From the crypts of the extirpated tonsils of the same persons they occurred in 97 per cent. in large numbers. In adults, the hemolytic streptococci occur four times as frequently in nontonsillectomized as in tonsillectomized throats (from 58 per cent. to 15.8 per cent.). These data illustrate that the faucial tonsils are important sources of hemolytic streptococci.

The nasopharynx and adenoid vegetations also harbor these bacteria.[2] They were recovered in 55 per cent. of swab cultures of the nasopharynx and the surface of the adenoids. In the extirpated adenoids the hemolytic streptococci were found in 61 per cent. of 103 children, aged from 5 to 16 years. They were particularly prevalent in the depths of the folds and in the crypt-like depressions. From these findings it is apparent that, as in the faucial tonsils, the hemolytic streptococci prefer the folds and crypts for their growth.

INCIDENCE OF HEMOLYTIC STREPTOCOCCI

The present study was undertaken to determine the incidence of hemolytic streptococci in children under 6 years of age. The patients

* Received for publication, Aug. 7, 1925.

* From the Michael Reese Dispensary, Sarah Morris Hospital, and the Department of Pathology and Bacteriology, University of Illinois, College of Medicine.

1. Pilot, I., and Davis, D. J.: Hemolytic Streptococci in the Faucial Tonsil and their Significance as Secondary Invaders, J. Infect. Dis. **24**:386-399 (April) 1919.

2. Pilot, I., and Pearlman, S. J.: I. Hemolytic Streptococci of the Adenoids, J. Infect. Dis. **29**:47-66 (July) 1921.

were afebrile and presented hypertrophic tonsils and adenoids. There was simple hyperplasia of the lymphoid tissue without fibrosis. Grossly they were enlarged, and contained no distinct purulent exudate in the crypts or follicles. The tonsils were wrapped in sterile gauze and cultures were made from them within five hours after excision. Only tonsils that were thoroughly enucleated were examined in order to obtain uncontaminated cultures of the crypt contents. Each tonsil was incised with a sterile knife and the bottoms of the crypts were exposed. Cultures were made with a loop from 3 to 4 crypts, and in a few instances separate cultures were also obtained from the surface. Inoculations were made into meat infusion agar (p_H 7.6), to which defibrinated blood was added in proportion of 1 of blood to 10 of agar. The blood agar was then poured into petri dishes, incubated aerobically at 37.5 C. and observed at the end of twenty-four and forty-eight hours for colonies of hemolytic streptococci. Small, round, discrete colonies surrounded

TABLE 1.—*Incidence of Hemolytic Streptococci in the Extirpated Tonsils of Children Aged from 2 to 6 Years*

Age	Number Examined	Number Positive	Number Negative
2 to 3 years	6	5	1
3 to 4 years	12	10	2
4 to 5 years	6	6	0
5 to 6 years	4	4	0
Total	28	25	3

Male, 17; female, 11.

by a clear zone of hemolysis from 2 to 4 mm. wide, which microscopically showed no red blood corpuscles at the end of twenty-four hours, were considered streptococci of the beta type of Smith and Brown.

The results of the cultures made from the tonsils of twenty-eight children, aged from 2 to 6 years, are indicated in Table 1. Hemolytic streptococci were found in twenty-five of twenty-eight (89.3 per cent.) in one or both tonsils. In nine instances the organisms were predominant and in three were present in pure culture in the crypts. As in the previous studies,[1] it was noted that on the surface of the tonsils the organisms were fewer than in the crypts. The associated flora consisted of a few hemolytic streptococci of the alpha type, constant numbers of *Streptococcus viridans,* pneumococci, hemolytic and nonhemolytic staphylococci, diphtheroids and gram-negative cocci.

The adenoid vegetations of eleven children, aged from 2 to 6 years, were removed and collected in sterile gauze. They consisted of hyperplastic lymphoid tissue from 1 to 1.5 cm. square and from 0.5 to 1 cm. thick. Most specimens presented distinct folds and crypt-like depressions. From these situations cultures were made employing the same

technic and mediums as for the tonsils. Six of the eleven (55.5 per cent.) were positive for hemolytic streptococci. In the adenoids of three children, aged from 2 to 3 years, two were positive, one was negative; in six, aged from 3 to 4 years, three were positive and three were negative; in two, aged from 4 to 6 years, one was positive and one was negative.

A further study was made of the incidence of hemolytic streptococci in the throats of normal children, aged from 6 weeks to 10 years. The children were seen in dispensaries; the infants were largely nutrition patients in the hospital or outpatient department. Swab cultures were secured separately from the pharynx and each tonsil, and were inoculated into melted blood agar. Thirty-six of seventy-five persons (47.7 per cent.) gave positive cultures from one or both tonsillar surfaces and nineteen (25.3 per cent.) from the pharynx (Table 2). Two infants, aged 6 weeks, both gave positive cultures. In practically all instances

TABLE 2.—*Incidence of Hemolytic Streptococci in Throats of Children Aged From 6 Weeks to 10 Years (Swab Cultures)*

Age	Number Examined	Number Positive	Number Negative
Under 6 months	11	5	6
6 to 12 months	10	7	3
1 to 2 years	21	11	10
2 to 4 years	11	4	7
4 to 6 years	5	3	2
6 to 10 years	17	6	11
Total	75	36	39

Male, 48; female, 27.

the number of hemolytic streptococcus colonies constituted less than 10 per cent. of the total number of colonies on the plate. These findings were in accordance with our previous results.[1]

The streptococci were isolated in pure cultures and their fermentative properties and pathogenicity determined. In infusion carbohydrate broth they formed a granular or flocculent sediment with fairly clear supernatant fluid. All fermented lactose and salicin; only two fermented mannite; none fermented insulin. According to Holman's classification, all but two strains correspond to *Streptococcus pyogenes*. Five strains were selected at random and, using 2 c.c. of a forty-eight hour ascites broth culture, were injected intravenously into young rabbits. All developed purulent arthritis within four days, and in one a marked thrombo-ulcerative endocarditis of the mitral and aortic valves with multiple infarcts of the spleen and kidney was encountered. These strains in their morphology, fermentation properties and pathogenicity resemble the streptococci isolated from older children and from many other sources.[1]

COMMENT

These results conform with our observations on the incidence of hemolytic streptococci in children, aged from 5 to 16, and in adults. It is evident that these organisms are found commonly at all ages. Their common occurrence would indicate that they are to be considered normal inhabitants of the throat, residing chiefly in the crypts of the tonsils and adenoids. They are to be considered the important and common bacteria for the development of infections of the lungs, pleurae, middle ears, sinuses, joints and endocardium, especially when local or general resistance is lowered by an acute specific infection or by a chronic debilitating disease.

CONCLUSIONS

1. Hemolytic streptococci were recovered in large numbers from the excised tonsils of twenty-five of twenty-eight children (89.3 per cent.), aged from 2 to 6 years; from the adenoids of the same children in six of eleven (55.5 per cent.).

2. From swab cultures of comparatively normal throats of seventy-five children, aged from 6 weeks to 10 years, hemolytic streptococci were found in sparse numbers in thirty-six (47.7 per cent.).

3. In young infants and children as in adults, these organisms reside normally in the tonsils and adenoids. From these sources the streptococcal complications in the course of other diseases commonly arise.

ENLARGEMENT OF THE SPLEEN IN MEASLES*

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The following observation concerning enlargement of the spleen during the eruptive stage of measles was made during the winter of 1922, and was reported at a meeting of the St. Louis Pediatric Society, Oct. 26, 1923. Two hundred sixty-four cases of measles made up the series on which conclusions were based. It was, however, deemed wise to repeat the study in some later epidemic of this disease before publishing the data then acquired, and to this end an additional 133 cases were observed during the winters of 1923 and 1924, the information obtained on this point being added to the original paper in Chart 2.

It is, of course, a common thing in clinical work to encounter a spleen that can be felt below the costal margin, but the almost abrupt appearance of the spleen during the eruptive stage of measles, and the suddenness of its disappearance as the rash subsided was quite unexpected and prompted an inquiry into the frequency of this phenomenon in this disease.

Bibliographic reports on this point were rather curious, for of a group of eleven textbooks on pediatrics, picked up more or less haphazard, eight made no allusion to the spleen in measles and three referred to it as follows: "the spleen is not palpable," "the spleen commonly shows no demonstrable enlargement" and "the spleen is not affected in measles and shows no appreciable enlargement." Six of these books were American, three were English and two were German.

In eleven of fourteen books on medicine, no reference to the spleen appeared in the clinical description of measles. In one of the remaining three it was said that "the spleen is not enlarged;" another stated that "enlargement of the spleen cannot be made out or only to a slight degree, if at all" whereas the third in contrast to these, namely, Osler and McCrae's "Modern Medicine," stated that "the spleen is usually slightly enlarged in measles."

Three books on diseases of the skin made no reference to this point, although of three books on pathology, one said that in cases of measles coming to necropsy "there is usually a moderate acute splenic tumor." This statement contrasted so pointedly with the various clinical descriptions quoted in the foregoing, that a second search was undertaken through the books on pediatrics and medicine in that part devoted not to symptoms but to morbid anatomy. In the twenty-eight

* Received for publication, Sept. 8, 1925.

* From the Department of Pediatrics, Washington University School of Medicine and the St. Louis Children's Hospital.

books, twenty-three did not describe a change in the spleen, but five referred to it as follows: one, a book on pediatrics, said "the lymphoid tissues of the spleen exhibit decided cellular hyperplasia" in measles; one of the books on medicine said "the spleen is, as a rule, swollen" in measles and a third said that "an acute hyperplasia of the spleen" occurs in this disease. The fourth of these books stated that "the spleen may show slight enlargement as the result of congestion," and the last that "the spleen is moderately swollen in measles, although this is more often determined at necropsy than at the bedside." In a word, it was interesting to note that there was discrepancy between the view of the clinician and the pathologist on this matter.

PREVALENCE OF MEASLES

Measles was prevalent in St. Louis during the year 1922, and abundant opportunity was presented for carrying through an observation on this point. All of the 264 patients examined were children under 12, a majority being under 7. They were seen at the City Hospital, the Mission Free School and in my private practice.

In compiling the percentage of positive tests for individual days from the day preceding the rash to the sixth day, every instance in which an enlarged spleen could be accounted for in some other way was removed from the series altogether; in this way typhoid fever, active syphilis and tuberculosis occurring coincidentally with measles served to eliminate seventeen positives which would otherwise have been counted. This was done, of course, in a desire to get a fair gage of the percentage which might justly be attributed to measles itself, although it is probable that, because of this, somewhat lower percentages may be reported here than is correct.

To summarize the tables which are adequately presented in Chart 1, it was found that of forty-seven patients with measles who were examined the day before the rash appeared, the spleen was found to be enlarged in 2 per cent. Of fifty-eight patients examined on the first day of the rash, the percentage rose abruptly to 24, and of eighty examined on the second day, the spleen was palpated in 43 per cent., or almost twice the number of positives encountered on the first day, it being quite often as large again as it was on that day. Sixty-five patients were examined on the third day of the rash and enlarged spleens were discovered in thirty-eight, three of these being eliminated, leaving thirty-five in sixty-two, which is 56 per cent., or slightly more than half of the patients seen on that day. On the fourth day there were forty-nine patients with a percentage of positives of 52, the spleen being of about the size noted on the third day and reaching commonly 1, 2 or even 3 cm. below the ribs.

On the fifth day of the rash the proportion of positives dropped abruptly to 25 per cent., thirty-six patients being examined, the spleen having diminished as rapidly in size after the fourth day as it had increased between the first and third days. Thirty-six cases were seen on the sixth day, with positives in 25 per cent., the size of these, however, being less, on the whole, than on the day before. During convalescence, that is, during the two weeks following the disappearance of the rash, opportunity was presented for examining a large group namely, 138 patients, and among these the spleen was palpated at or below the costal margin in twenty-two, or about 15 per cent.

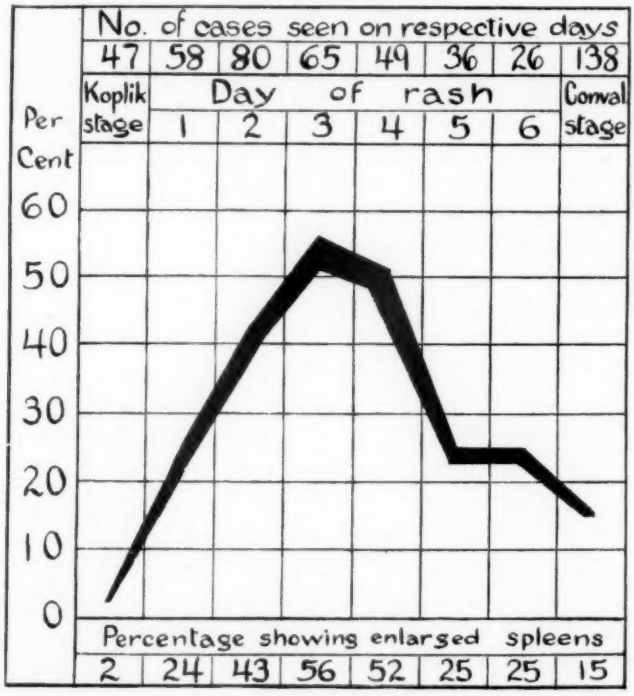

Chart 1.—This represents the occurrence of enlargement of the spleen during the eruptive stage of measles in a group of 264 cases occurring in St. Louis during the winter of 1922. The thickness of the line is intended to indicate the relative degree of enlargement noted on respective days.

COMMENT

In seeking to determine whether enlargement of the spleen is of any diagnostic value in measles, and occurs often enough to be included in the symptomatology of this disease, several factors must be reckoned with. The first thing, of course, is whether the enlargement noted was due to an intercurrent or complicating disturbance such as otitis, sepsis

or pneumonia. Cases of this sort were, therefore, tabulated in separate groups without discovering, however, that such an influence existed; to check this point further, spleens were felt for in a group of cases of otitis and of pneumonia, respectively, in children who did not have measles, the otitis group showing 6 per cent. positives and the pneumonia group 13 per cent., neither being sufficiently high to be of any particular importance. It is also noteworthy that the time of enlargement of the spleen in this series preceded by a considerable period the time in which such complications as otitis and pneumonia usually occur.

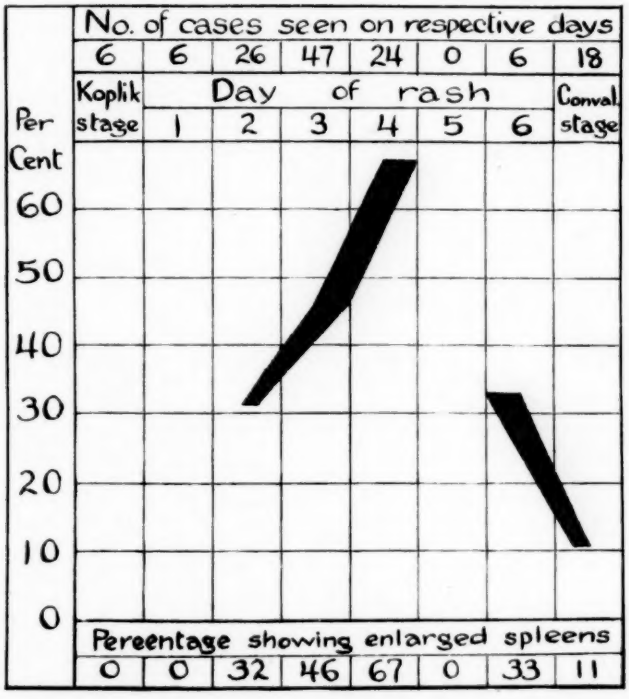

Chart 2.—This represents the occurrence of enlargement of the spleen during the eruptive stage of measles in a group of 133 cases occurring in St. Louis during the winters of 1923 and 1924.

The prevailing type of measles among these children, as well as in the entire epidemic in St. Louis of which they were a part, was singularly mild, at least so far as mortality figures may be used to indicate this, which shows that the septic phase had apparently little to do with the condition. Observation in individual cases seemed to bear this out, enlarged spleens occurring quite as well in the patients with a mild course as in the more severe cases.

CONCLUSIONS

From the foregoing the following conclusions may be drawn:

1. Enlargement of the spleen was found to occur in a majority of two independent groups of cases of measles, seen during three succeeding winters in St. Louis, and numbering altogether almost 400 persons.

2. This enlargement of the spleen was coincidental with the eruptive stage of this disease, both as to appearance and disappearance, the greatest enlargement both as to frequency and size being noted on the third and fourth days of the rash.

3. Contrary to what might be expected, the severity of an attack in these patients did not seem to make the occurrence of enlargement of the spleen higher than was found to be the case in those that ran a milder course.

4. These three conclusions run together, and indicate that enlargement of the spleen in measles is directly related to the virus of this disease.

5. It would, therefore, seem fit to include enlargement of the spleen in the symptomatology of measles.

CONGENITAL CARDIAC HYPERTROPHY

CASE REPORT *

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AND
A. H. ZEILER, M.D.
LOS ANGELES

Congenital cardiac hypertrophy—so called—is sufficiently rare, according to the literature, to warrant recording another case. Howland [1] has reported five cases and up to 1919 gathered reports which, including his own, made a total of twenty cases. Carrington and Krumbhaar [2] report a case in an infant, aged 12 months.

REPORT OF CASE

History.—Our patient, a girl, aged 5 weeks, was referred by Dr. W. R. Franklin because of gastro-intestinal disturbance, dyspnea and cyanosis. She was the second child, delivered normally, weighing 8 pounds, 2 ounces, and was breast fed most of the time. She passed from five to six green curd-like stools daily. On June 8, she had her first attack of dyspnea, and on defecation or passing flatus, perspired profusely. On June 10 she had another attack of dyspnea.

We first saw her on June 11, when her temperature was 100 F., her weight, 8 pounds, 2 ounces, as at birth, some jaundice and on crying, cyanosis. The bony thorax was prominent anteriorly with no pathologic changes in the lungs, and the heart showed no apparent abnormality. The lower edge of the liver was down to the level of the umbilicus. The remainder of the examination showed nothing of importance.

A tentative diagnosis was made of a congenital heart defect, because of the cyanosis on crying, dyspnea and enlarged liver.

A week later the patient showed a gain in weight, slept better, had fewer stools but tired easily while nursing and wheezed afterward. Breast feedings had been complemented. The liver had decreased in size and there was less jaundice and cyanosis. The lungs and heart still showed no apparent abnormality.

On June 23, the infant started to vomit, the extremities were cold, the respirations were grunting and the patient was cyanotic. The temperature was 97.8 F., and the pulse was 172. The lungs were clear though somewhat hyperresonant, but the heart dulness was now noted to be increased from the right to the left midclavicular lines. At the second intercostal space it was 6 cm. wide, and was 9 cm. at the nipple line. No murmurs were heard. The liver was enlarged, but there was no enlargement of the thymus.

The roentgenogram showed that the heart was enlarged to the right, the liver was enlarged, but there was no enlargement of the thymus.

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* Received for publication, Sept. 18, 1925.

* From the Pediatric and Pathologic Departments of the California Lutheran Hospital.

1. Howland, J.: Idiopathic Hypertrophy of the Heart in Young Children, Contributed to Medical and Biological Research. Dedicated to Sir Wm. Osler, Vol. 1, Johns Hopkins Press, 1919.

2. Carrington, G. L., and Krumbhaar, E. B.: So Called Idiopathic Cardiac Hypertrophy in Infancy, Am. J. Dis. Child. **27**:449 (May) 1924.

The baby died at 2 p. m., June 24, and at necropsy the heart was found to weigh 55.4 gm., and was 6.5 cm. (2½ inches) wide. There was marked hypertrophy of the ventricular musculature. The ductus Botalli and foramen ovale were closed, and all the valves were competent. The left auricle was normal in size but the right was dilated. There was a slight increase in the pericardial fluid. The lungs had some hypostasis, and the thymus was normal in size for the age. The abdominal organs were normal except for the enlarged liver and passive congestion in the kidneys.

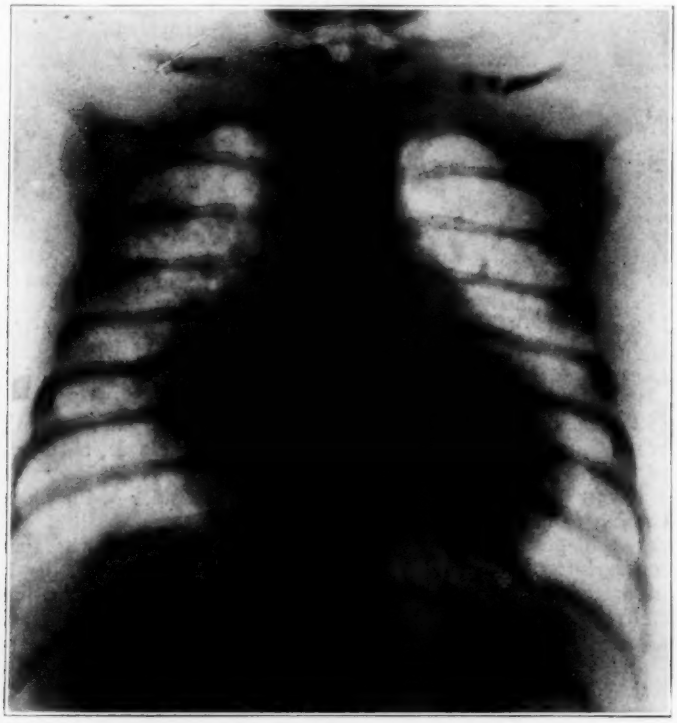

Fig. 1.—Roentgenogram shows increased shadow of heart to right as well as to left side.

SUMMARY

The normal weight for a heart in the second month is 19.6 gm.[3] This heart was similar to that of an infant aged 18 months. There is no etiology to explain this condition other than that it is congenital. The symptomatology is not marked, except for the rapid respirations or dyspnea in the late stages of the condition.

3. Boviard and Nichol: The Weights of the Viscera in Infancy and Childhood with Special Reference to the Weight of the Thymus Gland, Arch. Pediat. **23**:641 (Sept.) 1906.

In our patient, at the first examination, we did not note any increase in the cardiac outline which was later very evident, due probably to acute dilatation. The roentgenogram and necropsy findings showed that the heart must have been enlarged all the time but dilated antemortem.

Figure 2

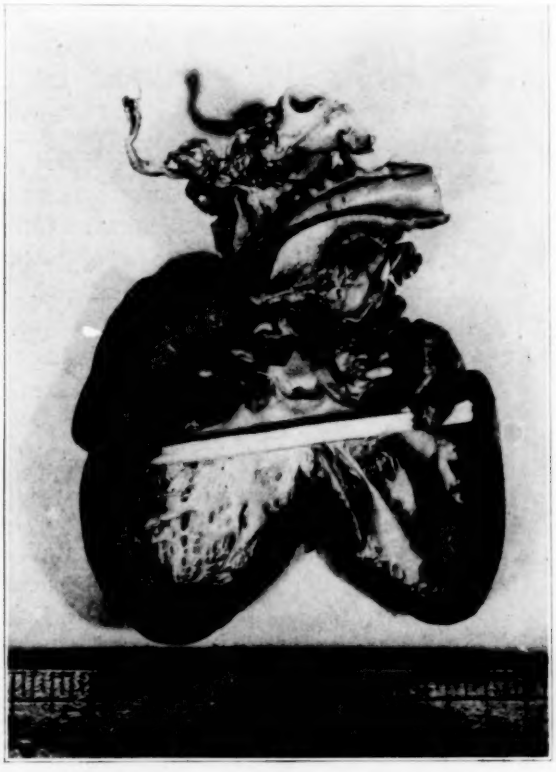

Figure 3

Fig. 2.—Photo does not show exact size present before being sectioned.

Fig. 3.—Heart sectioned through left chambers to show thickness of walls.

The liver changes were due to passive congestion, which also caused the digestive disturbances and cyanosis. The necropsy findings showed no nephritis.

CALCIFICATION OF SUBCUTANEOUS TISSUE IN A CHILD (CALCINOSIS UNIVERSALIS)

CASE REPORT *

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AND
JOSEPH DERBY, M.D.
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The presence of multiple calcified plaques in the subcutaneous tissue of children is a rare disease process. The few cases studied are so strikingly similar as to constitute a rather definite clinical and pathologic entity. The finding of pathologic calcification in tissues or organs is interesting both from a clinical and from a pathologic point of view. Often, clinically, the occurrence of tumor nodules composed of calcareous material presents a problem of diagnosis, usually not correctly made until roentgenograms have been taken. Pathologically, the presence of lime-salt aggregations is the end-result of a chronic disease process, in which, usually, there are no indications of the initial injury and the subsequent sequence of events. The deposition of calcium salts, associated with previous injury to fat, appears to be fairly well understood. Lee and Adair,[1] studying traumatic fat necrosis in breast tissue, describe the microscopic details such as the presence of fatty acid crystals, foreign body giant cells and the proliferation of connective tissue. Lecene and Moulonguet [2] write about the process in great detail, particularly the acute stage. These authors were concerned with calcification of subcutaneous fat previously exhibiting fat necrosis.

A number of case reports of subcutaneous calcification are present in the literature. These usually have been in adults, and are associated with some accompanying disease process. Ducasse [3] reports the case of a woman, aged 50, with calcified areas in the skin over knee, elbow and finger joints. Logan [4] describes a similar case, in which Raynaud's syndrome was a prominent feature. In a general way, Langmead [5] reviews the presence of calcification in children, and points out certain similar characteristics noticed in scleroderma, sclerodactylia, calcinosis,

* Received for publication, Sept. 24, 1925.

* From the Departments of Pathology and Orthopedics of the Children's Hospital, and the Harvard Medical School.

1. Lee, B. J., and Adair, F. E.: Ann. Surg. **80**:670 (Nov.) 1924.
2. Lecene, P., and Moulonguet, P.: Ann. d'anat. path. **2**:193 (May) 1925.
3. Ducasse, R. R.: Calification of the Skin, with Unusual Findings, Arch. Dermat. & Syph. **7**:373 (March) 1923.
4. Logan, J. R.: Arch. Radiol. & Electroth. **28**:55 (July) 1923.
5. Langmead, F. S.: Arch. Pediat. **40**:113, 1923.

dermatomyositis and myositis fibrosa. He states that it is rare for calcification of the subcutaneous tissue to occur alone. Under the title of "calcinosis universalis," Verse [6] describes several cases, and stresses the early changes in the intercellular substance of the connective tissue. Tisdall and Erb [7] report two cases of calcification of subcutaneous tissue in children, in which blood calcium and phosphorus were normal. A case of multiple calcifications of the subcutaneous tissue in a child was reported from this clinic by Morse.[8] Recent examination of this patient showed marked ankylosis of the joints and extreme wasting. The rareness of the condition, and the probable evidence of having no association with previous fat necrosis have influenced us to report the following case:

REPORT OF CASE

History.—A boy, aged 5 years, was admitted to the children's hospital, Oct. 26, 1924, because of a painful knee and multiple subcutaneous nodules. The family history was negative. The patient was breast fed for two months, and then was successfully given Mellon's food. The first tooth appeared at 9 months, and the boy walked at 18 months. During 1921, the child had pertussis and four convulsions; in 1922 he had bronchopneumonia, and in 1923 he had lobar pneumonia.

The present illness dates back to two and one-half years prior to examination, when the mother noticed that the boy appeared weak, unsteady, and dropped to his knees on attempting to walk. About six months later, several small, painless swellings appeared under the skin over the crests of both tibiae. Other similar subcutaneous nodules developed at many other points. In April, 1924, the skin over the left tibia became red, indurated and ulcerated, with the extrusion of chalky material and pus. Shortly afterward, the wound healed. During the two weeks before admission, the left knee had become swollen and tender on the posteromedial aspect. Here the subcutaneous tissue contained numerous stony hard nodules.

The physical examination showed a fairly well developed and nourished boy who appeared ill. The left knee was flexed, favored and protected. There was no lymphadenopathy. The face was flushed and there was a slight elevation of temperature (100 F.). A soft systolic murmur was heard over the apex. The skin in many areas, particularly over the face, right shoulder and left knee, was coarse, rough and mottled. The various subcutaneous nodules varied slightly in detail, and resembled each other in general characteristics. These tumor-like swellings ranged in size from 0.5 to 3 or 4 cm. in longest diameter. The nodule was either firm, hard and intact, or was less firm, yielding and fragmented. Usually the new growth was freely movable, while a few areas were fixed in position. The adjacent skin and tissue did not appear to be widely involved. There were no indications of lymphatic metastases. The periphery of the nodule was usually ragged, with elongated stellate radiating processes. The left knee was swollen, red, hot and exquisitely tender. Similar nodules were present bilaterally in Scarpa's triangle, on the buttocks, extremities and around the shoulder joints.

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6. Verse, M.: Beitr. z. path. Anat. u. z. allg. Path. **53**:212, 1912.

7. Tisdall, F. F., and Erb., I. H.: Report of Two Cases with Unusual Calcareous Deposits, Am. J. Dis. Child. **27**:28 (Jan.) 1924.

8. Morse, J. L.: Calcification of the Skin in a Child, Am. J. Dis. Child. **22**: 412 (Oct.) 1921.

A roentgenogram showed multiple deposits of calcareous material in the subcutaneous tissue and within the left knee joint.

The laboratory studies showed normal blood calcium and phosphorus. Urinalysis, tuberculin and Wassermann tests were negative. Analysis of a portion of one of the subcutaneous nodules revealed the presence of calcium salts.

Fig. 1.—The coarse skin and outlines of subcutaneous nodules.

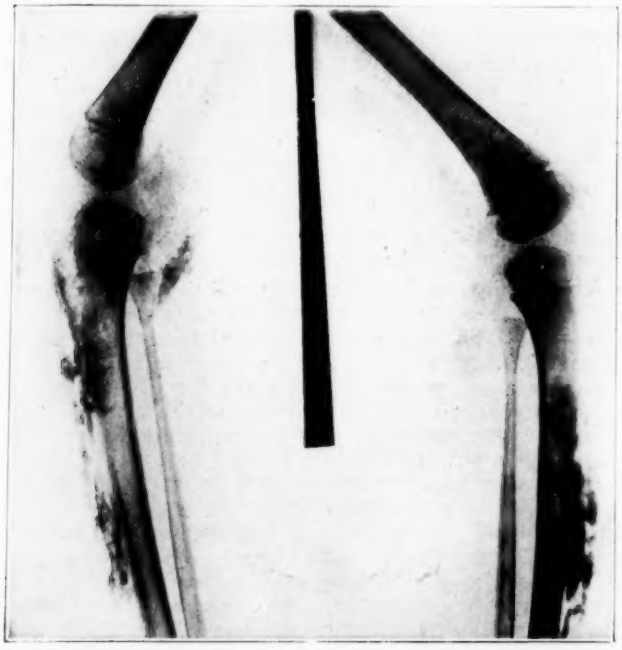

Fig. 2.—Roentgenogram, which shows numerous calcified plaques.

The next two months in the hospital was concerned with several minor changes. During a biopsy, the left knee was somewhat straightened. The biopsy wound healed readily. Several other calcareous areas broke down, with ulceration of the skin and extrusion of chalky material. Later, a diffuse cellulitis developed over the left shoulder.

Pathology.—Grossly, the specimen consisted of two pieces of skin and subcutaneous tissue measuring 2 by 0.5 cm. The epidermal surface of one piece was rough, red and dry. In the subcutaneous layer were deposts of chalky, hard material which measured 1.0 cm. in diameter. These depositions of lime were surrounded by fibrous and adipose tissue.

Microscopically, all sections were strikingly similar in appearance. The papillary layer of stratified squamous epithelium was irregular in outline and depth. There was considerable desquamation and cornification of the superficial layers. In a dense corium few hair follicles and gland structures were noticed. Portions of erector pili muscles were present. Small portions of fat within the corium were not altered.

Fig. 3.—The irregular papillae, dense corium and absence of calcium deposits.

As one passed into the subcutaneous layer, numerous thick-walled blood vessels came into view. The endothelium of these vessels was frequently conspicuous and bulged into the lumen. Others showed considerable fibroses of the arterial wall and perivascular lymphocytic infiltration. Some of these vessels were occluded by fibrous tissue.

The subcutaneous layer presented additional interesting changes. Between fat cells, and often at the periphery just within fat cells, depositions of a deeply basic staining granular material, were noticed. Often an entire lobule of fat was involved. However, often the calcium salt lies only between the

fat cells, while the inside of the cell is entirely empty. Here the lime formed a blue rim around the periphery of the adipose cell. Adjacent to the altered fat, broad bands of dense hyaline connective tissue containing new blood vessels and groups of lymphocytes were present. In some places, the deposition of lime appeared to extend from the fat into the connective tissue, while in other areas considerable lime was present in the connective tissue. The bulk of the lime salt lay in the fat and fibrous tissue of the subcutaneous layer.

There were no giant cells and no bone formation. No evidences of fatty acid crystal formation were seen; yet the sections showed collections of endothelial leukocytes, having a very granular cytoplasm, which were sometimes slightly vacuolated. Considerable amounts of fat were not calcified, but often

Fig. 4.—Photomicrograph, which shows obliterating endarteritis.

in such areas a pink eosin staining granular material was present in the connective tissue septums between fat cells. It was also noticed that the peripheral outlines of these fat cells were often represented by several interlacing or parallel wavy fibrillary strands, whereas in normal fat a thin line indicated the cell periphery. The connective tissue around the blood vessels and the nerves was not calcified.

COMMENT

Microscopic examination of sections made from biopsy tissue from this patient failed to reveal the presence of fat necrosis. There were

no indications suggesting the initial lesion. One really is at loss to explain the process of calcification. In some respects, the nature of the process resembles normal ossification. The hyaline connective tissue has become homogenous and forms a matrix similar to that prepared by cartilage cells. The granules of lime salt are deposited in this intercellular substance, and gradually coalesce to form areas of considerable size. Hofmeister [9] states that there is an absorption affinity between organic colloids and crystalline substances in solution. Wells [10] found

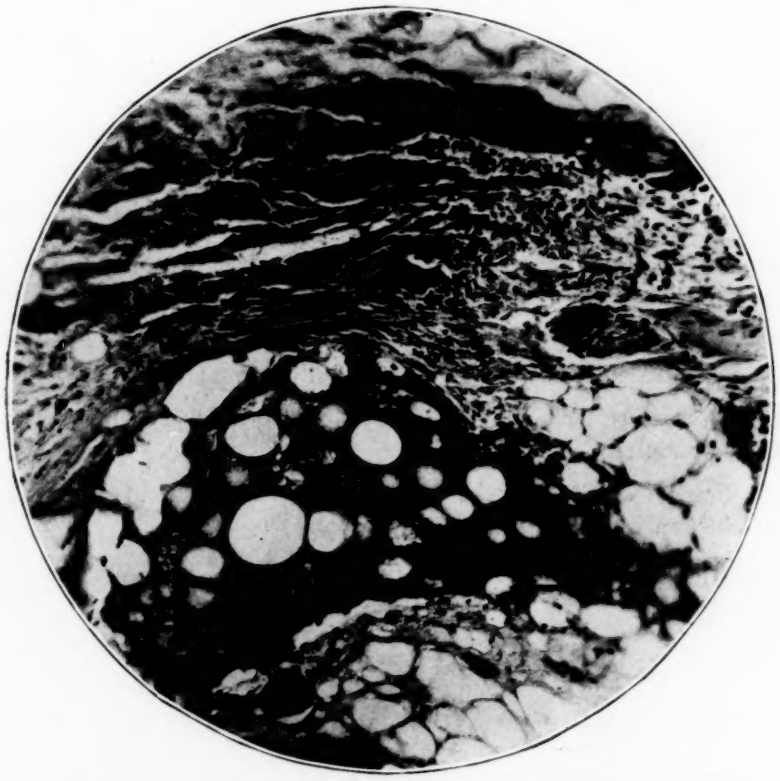

Fig. 5.—Photomicrograph, which shows extensive deposition of lime salt both in fat and in fibrous tissue. Groups of lymphocytes lie between.

that the ratio of calcium carbonate and phosphate is the same in normal ossification and in pathologic calcification.

In our case and in other cases reported, there was a variable degree of obliterating endarteritis, some of the patients even exhibiting Raynaud's syndrome. Circulatory disturbances appeared to be an early complaint in a number of such patients. The hyaline degeneration of

9. Hofmeister, F.: Arch. f. exper. Path. u. Pharm. **28**:210, 1891.
10. Wells, H. G.: Chemical Pathology, Ed. 2.

the subcutaneous connective tissue may probably be accounted for by improper blood supply or nourishment. However, the endarteritis and hyaline connective tissue may be resultant to a common cause.

Lichtwitz [11] calls attention to the possible part proteins may play in the induction of calcification. He thinks that precipitation of colloids in degenerated tissues may bring about a reduction in soluble crystalloids, whereby the more insoluble salts, such as calcium, are precipitated.

Virchow recognized a group of cases manifesting multiple calcifications, in conditions in which considerable destruction of bone has been taking place. Usually, the depositions are in various organs, particularly the wall of the stomach. In our case, the blood calcium was normal, and there were no evidences of involvement of organs.

Regardless of how speculative the repeated foregoing remarks have been, we cannot help but feel that definite physiochemical factors of local importance have influenced the depositions of calcium, since there are no evidences of fat necrosis, and the blood calcium was normal.

SUMMARY

1. A case of multiple calcifications of the subcutaneous connective tissue and fat, apparently unassociated with fat necrosis, is reported.

2. Other cases of single and multiple depositions of lime salts are referred to in the literature.

3. Several known hypotheses are repeated in an attempt to explain the induction of calcification.

11. Lichtwitz, L.: Deutsch. med. Wchnschr. **36**:704, 1910.

VARIATIONS IN THE ANTISCORBUTIC PROPERTIES OF DRY MILK*

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The information regarding the vitamin potency of milk and milk products which has become available during the past decade has been of no little interest to those concerned with the intricate problems of infant feeding. Many of these investigations, while of a purely empirical nature, have, nevertheless, served as a basis for a more accurate appraisal of the nutritive merits of the different products than was possible before. Since this paper is chiefly concerned with the antiscorbutic potency of milk in dry or powdered form, only the conclusions from a few of the significant investigations pertaining to this dietary factor in milk will be cited.

REVIEW OF THE LITERATURE

The data from different laboratories have shown that the antiscorbutic property of milk is not of constant and uniform potency. Cohen and Mendel [1] found that 70 c.c. of fresh raw milk fed daily afforded guinea-pigs complete protection from scurvy, whereas 50 c.c. quantities failed to do so. Hart, Steenbock and Smith [2] state that an average consumption of 84 c.c. of raw whole milk per day provided absolute protection and that 30 c.c. of the same milk delayed the onset of the disease. Hess and Unger [3] state that 80 c.c. of fresh milk per day furnishes adequate protection for the guinea-pig. Chick, Hume and Skelton [4] report adequate protection only when from 86 to 130 c.c. was fed. Barnes and Hume [5] found that 98 c.c. daily was insufficient to prevent scurvy, and that from 119 to 147 c.c. quantities were necessary to effect a cure.

The variable amounts of milk found necessary to protect guinea-pigs from scurvy may easily be explained by the difference in potency of the milk as caused by the amount of vitamin C in the feed of the lactating animal. Hart, Steenbock and Ellis [6] report that 50 c.c. per day of milk

* Received for publication, Sept. 24, 1925.
* From the Research Laboratories of The Dry Milk Company, New York.

1. Cohen, B., and Mendel, L. B.: J. Biol. Chem. **35**:425 (Sept.) 1918.
2. Hart, E. B.; Steenbock, H., and Smith, D. W.: J. Biol. Chem. **38**:305 (June) 1919.
3. Hess, A. F., and Unger, L. J.: J. Biol. Chem. **38**:293 (June) 1919.
4. Chick, H.; Hume, E. M., and Skelton, R. F.: Biochem. J. **12**:131, 1918.
5. Barnes, R. E., and Hume, E. M.: Biochem. J. **13**:306, 1919.
6. Hart, E. B.; Steenbock, H., and Ellis, N. R.: J. Biol. Chem. **42**:383 (July) 1920.

produced in the summer was adequate for complete protection, whereas from 75 to 80 c.c. was necessary when milk produced in the winter was used. Dutcher and his co-workers [7] found that 20 c.c. per day of summer milk was equivalent in antiscorbutic potency to 60 c.c. of winter milk, but that both quantities were inadequate for protection. They found, however, that from 70 to 80 c.c. of winter milk gave satisfactory protection. Hess and his collaborators [8] have also clearly shown that wide variations in the vitamin C content of milk may result from differences in the ration fed during the period of lactation.

Aside from the variability in antiscorbutic potency of milk, caused by inherent variations in the ration of the cow, other factors introduced by the processing of milk apparently influence the potency of vitamin C in this product. The work of Hess and Weinstock [9] shows that the contamination of milk by small amounts of copper during pasteurization diminishes its antiscorbutic properties. The results which have been obtained from desiccated milk indicate that the methods of drying affect the potency of this vitamin in such products. The observations of Hess and Unger,[10] Hart, Steenbock and Ellis,[11] Johnson and Hooper,[12] and Jephcott and Bacharach [13] are in close agreement in regard to the relative antiscorbutic properties of dry milk made by the Just process, and that made by the spray method. The conclusions reached by these investigators is to the effect that the roller process powder, especially certain brands, shows little or no reduction in antiscorbutic value as compared with natural fluid milk, whereas the spray process products in most instances show a marked diminution of this factor. The difference in results obtained from milk powder prepared by the two methods has been frequently attributed to the difference in degree of oxidation to which each of the products are subjected during desiccation. This hypothesis is supported by different investigations which have clearly demonstrated the deteriorating effect of oxidation on this vitamin. Cavanaugh, Dutcher and Hall,[14] however, have recently reported a high degree of protection from scurvy for guinea-pigs, with as low as 40 c.c. per day of reconstituted spray process powder produced from milk of

7. Dutcher, R. A.; Eckles, C. H.; Dahle, C. D.; Mead, S. W., and Schaefer, O. J.: J. Biol. Chem. **45**:119 (Dec.) 1920.

8. Hess, A. F.; Unger, L. J., and Supplee, G. C.: J. Biol. Chem. **45**:229 (Dec.) 1920.

9. Hess, A. F., and Weinstock, M.: J. A. M. A. **82**:952, 1924.

10. Hess, A. F., and Unger, L. J.: Am. J. Dis. Child. **17**:221, 1919.

11. Hart, E. B.; Steenbock, H., and Ellis, N. R.: J. Biol. Chem. **46**:309 (April) 1921.

12. Johnson, J. M., and Hooper, C. W.: U. S. Public Health Rep. **37**:989 (April 28) 1922.

13. Jephcott, H., and Bacharach, A. L.: Biochem. J. **15**:129, 1921.

14. Cavanaugh, G. W.; Dutcher, R. A., and Hall, J. S.: J. Indust. & Engin. Chem. **16**:1070, 1924.

late fall and early winter. As a result of their studies, they conclude that the spray method of drying causes no diminution in the antiscorbutic factor. Although a marked variation in the vitamin C content of milk may result from differences in the ration of the cow, the exact causes of the variations in protective ability of milk powders made by different methods are as yet not clearly explained. In view of the constantly increasing use of dry milk for infant feeding, the investigations recorded herein, which are the first of a series, were designed to ascertain, if possible, some of the reasons for the discordant results previously reported from this product.

EXPERIMENTAL DATA

In these experiments, attention has been given to the basal scorbutic ration and to the period of storage as possible factors contributing to the reported differences in the antiscorbutic potency of milk powders. The animals to be tested were carefully selected from the breeding colony, with the object of using only those of uniform age and weight. During the suckling period and until they were placed on experiment, they had access to a stock ration consisting of oats, casein, hay, salt, fresh whole milk and limited amounts of green vegetables given three times a week. This ration has been found adequate for the maintenance of the breeding colony, but probably does not permit the storage of a large surplus of the antiscorbutic factor.

The first series of experiments was designed to determine whether the differences in the antiscorbutic value of spray process powder could be attributed to the basal scorbutic ration used by different investigators. Two different rations were used. The first ration was the same as that used by Cavanaugh, Dutcher and Hall, and consisted of oats, 60; bran, 15; autoclaved alfalfa meal, 15; casein, 5; calcium carbonate, 1; sodium chlorid, 1, and butterfat, 3. The second ration was the same as that used by many other investigators, and consisted of rolled oats, 99; sodium chlorid, 1; and hay ad lib. The oats and hay were autoclaved for forty-five minutes at 15 pounds pressure. As the sole source of the antiscorbutic factor, reconstituted spray process whole milk powder (Klim brand) was fed in from 40 to 80 c.c. quantities daily. In certain instances, the 40 c.c. quantities was increased to 90 c.c. after scurvy symptoms had developed. In order to assure proper consumption of the milk, the animals were fed the unconsumed daily portion by pipet. The whole milk powder used for the experiments was purchased in the open market in one pound hermetically sealed tin containers, early in January, 1925, and from the information available it is believed to have been manufactured during the late summer of 1924.

From the records shown in Figure 1, it is to be noted that all animals receiving 40 c.c. of the reconstituted milk per day developed scurvy

within from eleven to twenty days, irrespective of the basal ration used. In all instances the dosage was increased to 90 c.c. per day soon after the first symptoms were observed. Three of the animals receiving the first ration died within a short period after receiving the increased dosage. In one case, life was prolonged for several weeks, but the animal was severely crippled with chronic scurvy and there was no indication that the 90 c.c. per day was affording any relief. On the

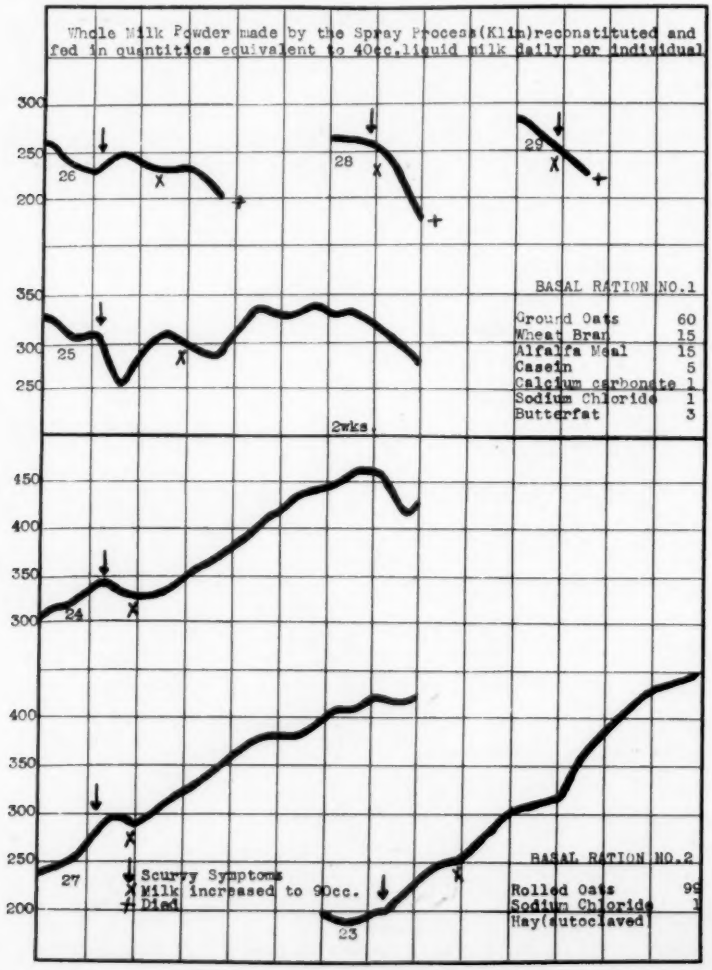

Fig. 1.—This chart shows the results obtained when 40 c.c. of reconstituted whole milk powder, made by the spray process (Klim), was used as the only antiscorbutic. All animals developed scurvy in less than three weeks. There was no abatement of the disease when the amount was increased to 90 c.c. The animals on Ration No. 2 lived longer and made substantial gains, but were badly crippled with chronic scurvy after having received the increased dosage for from ten to twelve weeks.

second ration, all of the animals that received the 90 c.c. per day soon after the first scurvy symptoms were manifested made substantial gains for a period of several weeks, but all were severely crippled in the hind quarters with chronic scurvy, which showed no signs of abatement during the period of observation. Figure 2 shows the condition of these animals after receiving the increased dosage for a period of from ten to twelve weeks. The records shown in Figure 3 are those obtained from feeding

Fig. 2.—The condition of three animals after having received 90 c.c. per day of reconstituted spray process whole milk for twelve weeks. All animals were severely crippled in the hind quarters with chronic scurvy, which showed no signs of abatement on the increased dosage of reconstituted milk powder.

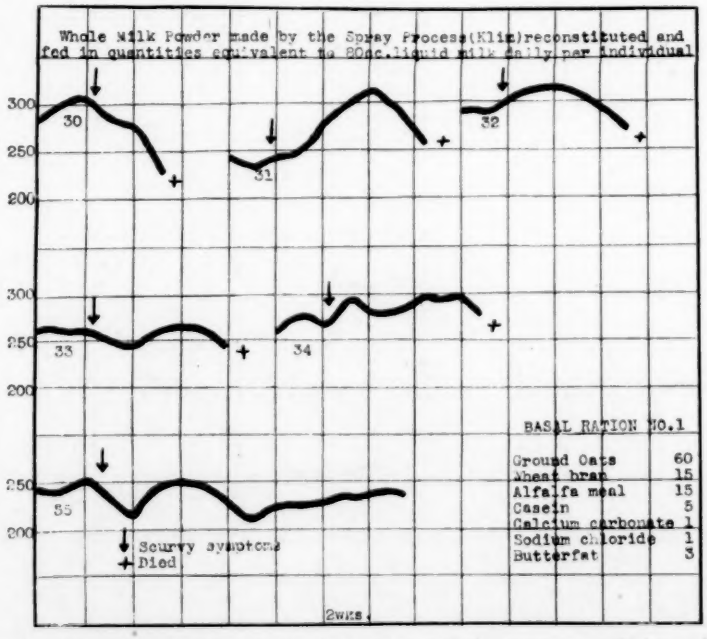

Fig. 3.—This chart illustrates the lack of a sufficient amount of the antiscorbutic vitamin in 80 c.c. of reconstituted milk powder made by the spray process (Klim) to protect guinea-pigs from scurvy. All animals developed the disease in less than three weeks, and all but one died within nine weeks.

80 c.c. per day of the reconstituted spray process powder as the sole antiscorbutic factor with the first basal ration. All animals in this lot developed scurvy within eighteen days, and all but one died within a period of eight weeks. No attempt was made to cure these animals by increasing the dosage. These records, as obtained from spray process

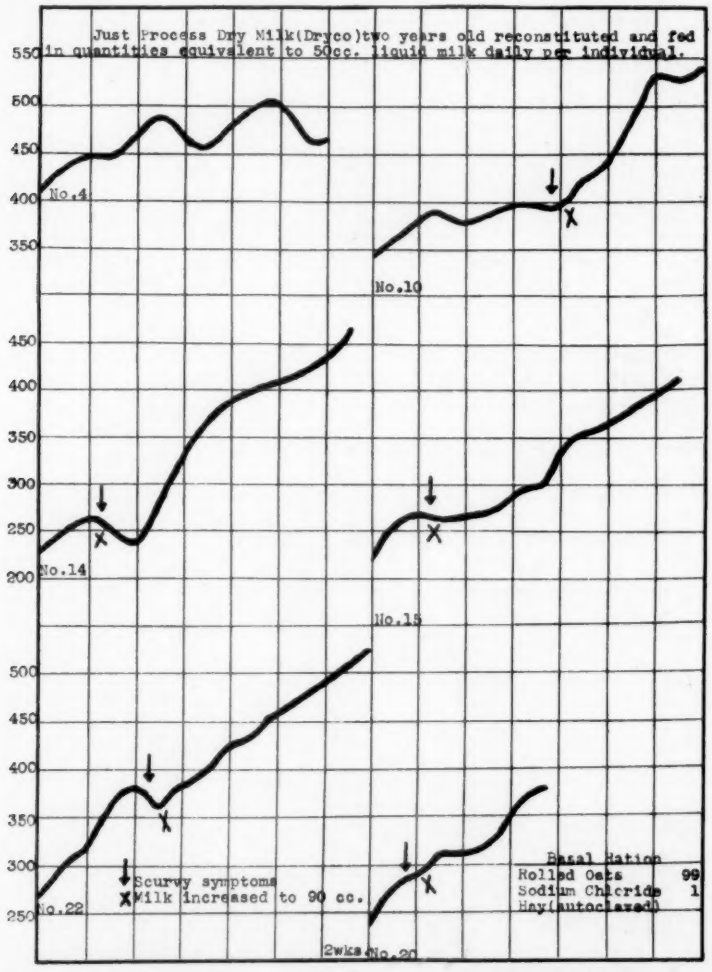

Fig. 4.—This chart shows that 50 c.c. of the reconstituted two year old Dryco was not sufficient to protect guinea-pigs from scurvy. The arrow indicates the incidence of scurvy. The cross shows where the amount of Dryco was increased to the equivalent of 90 c.c. liquid milk. This amount was found to effect a complete cure.

powder and recorded without selection, are in substantial agreement with those reported from numerous other sources. It seems apparent, therefore, that differences in the basal ration cannot be indicated as responsible for the discrepant results recorded heretofore.

Since oxidation is known to have a deteriorating effect on the antiscorbutic factor, a series of tests were conducted to ascertain whether a long period of storage tended to diminish this factor in powdered milk. The dry milk used for these tests was made by the Just process (Dryco

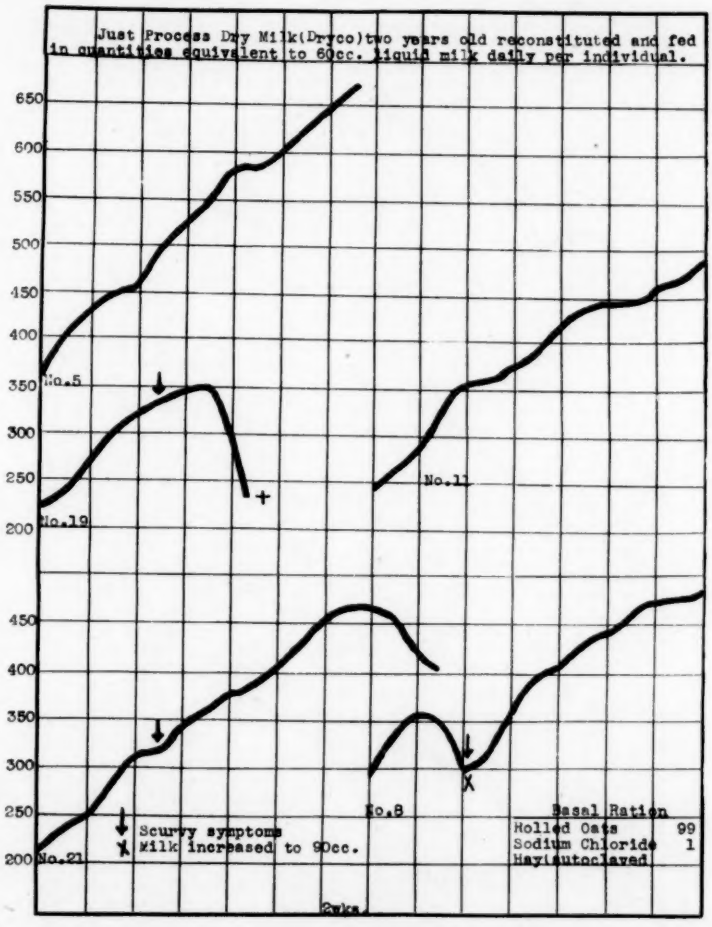

Fig. 5.—This chart shows that 60 c.c. of reconstituted two year old Dryco gave materially better protection from scurvy than the 50 c.c. quantity. Two of the individuals were completely protected. One developed mild symptoms that soon disappeared without additional antiscorbutic. One patient (No. 8) developed scurvy but was completely cured on 90 c.c. of the same milk powder. Another (No. 19) died prematurely, due to scurvy and to other complications.

brand), and consisted of small increments taken from the daily production of a commercial milk drying plant during the interval between September 18 and October 21, and, therefore, may be considered as representative of the commercial product manufactured during the early

fall when cows were receiving a ration of late vegetation, supplemented by a certain amount of stall feeding. Immediately after manufacture, the dry milk was placed in tin containers and hermetically sealed with normal air which occupied the interstices between the powder particles

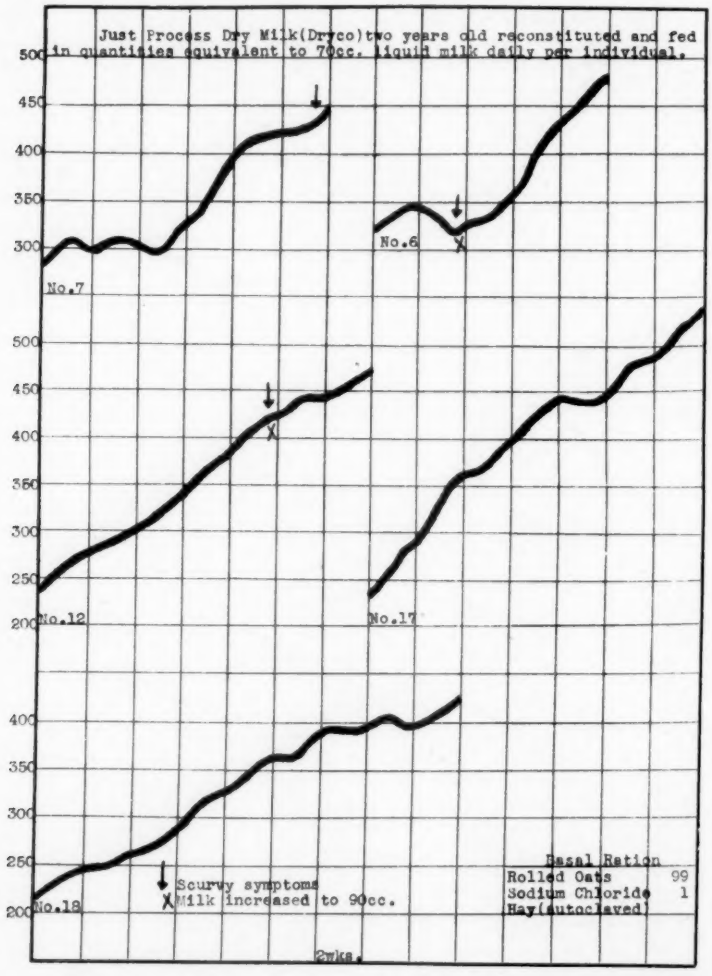

Fig. 6.—This chart shows that 70 c.c. of reconstituted two year old powder gave substantially the same results as 60 c.c. Two animals showed no signs of scurvy during the experimental period; two others showed slight symptoms after from ten to twelve weeks and one developed scurvy within three weeks.

to the extent of about 80 per cent. of the volume of the container. The sample tins were stored at room temperature on the laboratory shelves for a period of two years. At the end of this time, the daily increments were thoroughly mixed, and the mixed product was repackaged for use during the course of the experiments. The particular object in mixing

the product was for the purpose of eliminating any variations in the properties of the powder which might have resulted from unknown variations during the period the samples were collected and stored.

In conducting these feeding experiments, only the second basal ration previously mentioned was used. The sole source of the anti-

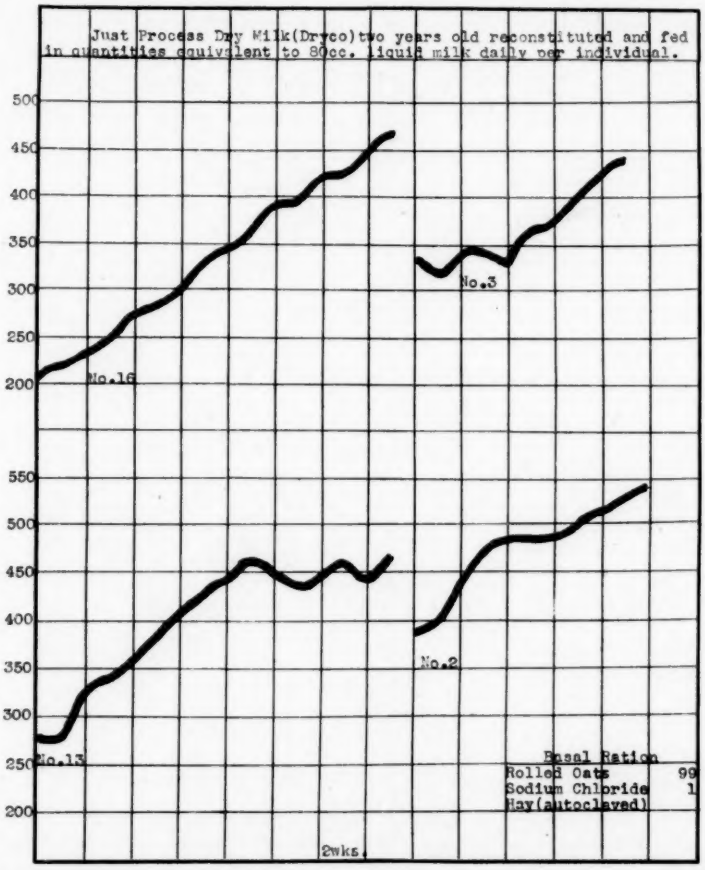

Fig. 7.—This chart illustrates the full protection against scurvy afforded by two year old, air packed Dryco when fed in a quantity equivalent to 80 c.c. of liquid milk per person daily. The same quantity of fresh raw milk or fresh dried milk is usually considered necessary to protect a guinea-pig from scurvy.

scorbutic factor was furnished by the reconstituted Just process milk, previously stored at room temperature for two years. Quantities varying from 50 to 80 c.c. of fluid milk equivalent were fed daily. Uniform milk consumption was assured by feeding with pipet an amount of reconstituted powder equivalent to the daily unconsumed portion. All animals which developed severe scurvy were given 90 c.c. of the reconsti-

tuted product each day thereafter, in order to ascertain whether the increased quantity would effect a cure. The results obtained from the various quantities are shown in Figures 4 to 7.

It is to be noted that most of the animals receiving 50 c.c. of the reconstituted milk developed scurvy within a period of from two to eight weeks (Fig. 4). When the quantity was increased to 90 c.c. per day after the development of severe scurvy symptoms, rapid improvement and ultimate recovery resulted. Two of the five animals receiving 60 c.c. per day (Fig. 5) showed no scurvy symptoms during the course of the experiments. One animal developed severe scurvy and was subsequently cured by increasing the dosage to 90 c.c. One animal (No. 21) developed mild scurvy symptoms after about five weeks, but subsequently recovered without receiving an increased dosage. When 70 c.c. (Fig. 6) of the reconstituted milk was given daily, the results were very similar to those obtained with 60 c.c. Two animals showed no signs of scurvy during the period of observation, whereas two others manifested unmistakable symptoms after a period of from ten to twelve weeks. One animal developed scurvy after three weeks, and was subsequently cured by increasing the amount of 90 c.c. per day. All the animals receiving 80 c.c. daily (Fig. 7) were successfully protected from scurvy throughout the observation period of from nine to fifteen weeks. Since these results obtained from Just process milk powder, stored for two years at room temperature and packed in an atmosphere of air, are in such close agreement with those reported from numerous other sources for fresh fluid milk, it is logical to assume that there was little or no diminution of the antiscorbutic factor as a result of desiccation or oxidation during the long storage period.

SUMMARY

Experiments are recorded which show that as high as 80 c.c. of reconstituted spray process whole milk powder per day is insufficient to protect guinea-pigs from scurvy, when either of two common basal scorbutic rations are used. The results are in substantial agreement with those of many other investigators, who report a deficiency of the antiscorbutic vitamin in desiccated milk made by certain spray processes.

The data also show that dry milk made by the Just roller process, and stored in an atmosphere of air at room temperature for two years, has an antiscorbutic potency substantially equivalent to that reported for fresh milk produced at the same time of the year.

It is concluded that neither the differences in the scorbutic basal ration nor the period of storage serves as an adequate explanation for the low antiscorbutic values reported for certain milk powders.

BRONCHIAL ASTHMA IN CHILDREN AND IN YOUNG ADULTS*

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In children, allergic disturbances of the respiratory tract are exceedingly frequent. It is probable that protein sensitization is at the basis of most recurrent head colds and of bronchitis, especially those which start without fever. Children who are sneezers, or who have wet noses continually, or who develop coryza or deep cough on the slightest provocation, usually are allergic subjects. It is well recognized that allergy causes hay-fever and asthma. In fact, as a general cause for illness in childhood, we agree with Shannon, who feels that allergy ranks next to infection, and that much infection is secondary to allergic congestion of the mucous membranes.

Bronchial asthma is the most serious of all respiratory disturbances due to allergy. Asthma is frequent in childhood, and is often mistaken for bronchitis or pneumonia. Such failure to recognize asthma endangers the life of the child because of the liability to repeated secondary infections such as sinusitis, tonsillitis or pneumonia.

This article is a report of 110 cases of bronchial asthma in children and in young adults. All have been seen in private practice during 1923 and 1924, and all have cooperated satisfactorily with us in their treatment for a minimum period of four months. Seventy-seven of these cases occurred in patients under 10 years of age, and thirty-three in patients between the ages of 10 and 20 years.

DIAGNOSIS

The occurrence of some type of allergy in the family history lends probability to a suspected bronchial attack being asthma. In our patients, 19.1 per cent gave a history of allergy on both sides of the family, and 51.8 per cent gave a unilateral family history of allergy. This total of 70.9 per cent, as contrasted with 58.4 per cent with a family history of allergy in our series [1] of 234 asthmatic patients of all ages, shows the great influence heredity plays in the development of asthma in youth.

The personal history of the patient is most important in the diagnosis of asthma. The history of difficult or labored respirations with bron-

* Received for publication, Oct. 3, 1925.
* Read before the California Medical Association, May, 1925.

1. Rowe, Albert H.: The Treatment of Bronchial Asthma, J. A. M. A. **84:** 1902-1905 (June 20) 1925.

chitis, or of a wheezing or noisy type of breathing with a dry or moist cough usually indicates bronchial asthma. Such a diagnosis is extremely probable if the patient gives the history of having or of having had hay-fever, urticaria, eczema, redness or itching of the eyes, sneezing and itching of the nose, itching of the pharynx, angioneurotic edema, allergic indigestion or other phenomena generally recognized today as due to allergy. The history, moreover, will frequently indicate the specific type of sensitization at the basis of the asthma. Histories of the food, animal emanation, pollen, orris root, as well as other miscellaneous types of asthma are very characteristic.

The physical examination clinches the diagnosis of asthma during the attack, revealing the prolonged expiration with the squeals and musi-

Occurrence of Skin Reactions to the Most Common Proteins Used in Testing One Hundred and Ten Patients with Asthma

Food Reactions	110 Cases	Percentage of Reactions
Wheat	24	21.8
Corn	4	3.6
Oats	4	3.6
Rice	7	6.3
Egg	23	21.0
Milk	12	10.9
Fish	9	8.2
Nuts	8	7.3
Meats	9	8.2
Fruits	17	15.5
Vegetables	34	31.0
Total food	59	53.6
Animal Inhalants:		
Feathers	64	58.2
Horse	23	21
Cat	19	17
Rabbit	16	14.5
Sheep	10	9
Silk	3	2.7
Total animal	79	71.7
Orris root	5	4.5
Tree pollen	7	6.3
Spring pollen	42	38.2
Fall pollen	26	23.6
Total pollen	44	40

cal sounds so pathognomonic of the disease. Between attacks, when desensitization has occurred, no indications of asthmatic breathing may be present and no other physical finding may be found. In such a period the probable diagnosis of asthma must be made on the history.

SKIN TESTING

Skin testing with proteins of the organic substances which may cause asthma either through inhalation, ingestion or absorption, offers a method for determination of the specific cause of the asthma. The most important proteins with which to test the patient are usually suggested by a careful history. However, we have found through experience that testing must be routine with the proteins of all foods, condiments, animal emanations, pollens and miscellaneous substances such

as orris root, pyrethrum and silk. When such routine testing is not done, an important sensitization is often overlooked, and as a consequence the asthma is not properly controlled. Specific proteins only have been used in our work. We feel that the use of so-called group proteins is not advisable. Not only must the testing be done routinely with a large number of proteins, but when a satisfactory explanation for the asthma is not obtained by testing, or the treatment indicated by the skin reactions does not control the asthma satisfactorily, careful retesting must be carried out. The necessity of retesting was first emphasized by Schloss, who demonstrated that after an allergic attack due to eggs, the skin reactions may entirely disappear until a recurrence of the attack. Formerly, we did not realize the importance of retesting, and many cases of asthma were diagnosed as nonsensitive because of negative skin tests. It is recognized now that the best time to test an asthmatic patient is just before or at the onset of an asthmatic attack, and that testing may have to be repeated several times before the skin reactions reveal all the sensitizations. Thus D. D., a girl, aged 10 years, had had attacks of asthma every one to two weeks steadily since the age of 2 years. She had been tested one year before in a careful manner, with positive reactions resulting to all cereals excepting corn, and to clam, walnut, pecan, banana, peach, tomato, potato and cocoa. However, her asthma had not been controlled. On retesting her, we obtained all the positive food reactions the other physician had found, as well as a definite reaction to orris root and delayed reactions to feathers. No asthma has occurred for six months, since treatment based on reactions to orris root and feathers as well as to foods has been carried out. Another important example of the value of retesting follows: J. P., a boy, aged 13, had had asthma all his life. He weighed 78 pounds, was thin, and appeared ill. Skin tests gave positive reactions to several proteins of wheat. Our exclusion of wheat from his diet had given complete relief from asthma for four months and the boy gained 15 pounds in weight. In April, he began to wheeze, and retesting showed definite pollen reactions which had been suspicious before. Specific pollen treatment gave relief.

POSITIVE SKIN REACTIONS

In analyzing the reactions obtained in our series of 110 cases of asthma in children and in young adults, we find that 95 per cent. of these patients gave one or more positive skin reactions. This high percentage of sensitive subjects is in sharp contrast to the results published by Walker in 1920, who found about 50 per cent. of his patients of the same age in his so-called nonsensitive group. Our higher percentage is probably due to the use of a large number of proteins in routine skin testing, and to the frequent retesting of doubtful cases. During the last

five years, moreover, a large number of pollen, food, animal emanation and miscellaneous proteins have gradually been added to our collection, so that today more than 400 proteins are available for skin testing.

A further analysis of our reactions in these 110 cases of asthma calls forth the following comments. Seventy-one and seven-hundreths per cent. of our patients reacted to proteins of animal emanations. Reactions to feathers were obtained in 58.2 per cent. of the series. Horse, cat, rabbit, and sheep wool gave reactions in 21, 17, 14.5 and 9 per cent. of our cases respectively. Of all the animal emanations, our results and clinical experience would indicate that feather proteins are the most important in the etiology of asthma. As with all reactions we feel that the protein may either cause the asthma, or be producing allergic coryza, or a mild type of bronchial spasm or be of purely potential danger. Because of the apparent ease of sensitization to feather protein, no child subject to allergy should sleep on them. The same assertion applies to hair mattresses. Pollen reactions have been obtained in 40 per cent. of our cases. This pollen factor in asthma is very important, and formerly was nearly entirely overlooked. With routine testing and retesting today, we uncover many cases of pollen allergy when no definite history of such sensitization is obtainable. The importance of food as a cause for asthma is emphasized by the fact that 53.6 per cent. of our series gave positive reactions. Wheat and egg proteins gave reactions in 22 and 21 per cent. respectively of our patients, and, with milk, are the greatest factors among the food proteins in the production of asthma. Vegetables gave reactions in 31 per cent. of the series, though asthma is probably seldom caused by such proteins. No bacterial proteins have been used in our work during the last two years for the following reasons. First, we feel that bacterial allergy is the sole basis of asthma in a very small number of cases, and second, we feel that the use of stock bacteria to determine a possible allergy to an autogenous bacteria is unscientific and unsatisfactory in practice. As a general observation, it is important to point out that multiple sensitization is the rule in nearly every subject of our series. Moreover, nearly every patient gave reactions to members of two or more of the large classes of proteins used in our investigations.

TREATMENT

The treatment of asthma in childhood and in youth must be based on the protein sensitization revealed by skin tests and history. Since nearly every subject has multiple sensitization at the basis of the asthma, the treatment is usually complex, and requires constant and watchful analysis by the physician as well as the most faithful and accurate cooperation by the patient.

Food Cases.—Food sensitization is a more important cause of asthma in childhood than in adult life. In our series, 53.6 per cent. reacted to foods. Though certain of these reactions, especially those from fruits and vegetables, were probably at the basis of hives or eczema, all reactions should be kept in mind as potential causes of asthma. Wheat, eggs and milk were found to be the foods most commonly causing asthma. The best treatment for such food sensitization is absolute exclusion from the diet. Since food allergy is frequently overcome in childhood through natural desensitization, it is probable that with total exclusion from the diet for one to two years, tolerance for the food may gradually return. Desensitization by the gradual feeding of the food as well as by hypodermic administration of the food protein, has been tried in our clinic. Our impression is that the latter method will probably yield good results.

Animal Emanation Cases.—Animal emanations gave positive reactions in 71.7 per cent. of our series, confirming our clinical impression that they play a large part in the production of asthma in childhood. Such sensitization is probably responsible for much of the perennial coryza, nasal itching and congestion which was present in 68 per cent. of these patients. The greatest care must be taken to remove all animal substances from the living environment of the susceptible asthmatic subject. This is especially necessary when the patient has asthma from the inhalation of house dust. The most common ingredients in house dust are from animal substances, such as horse and rabbit hair in upholstery, silk and wool in furnishings and carpets, feather in pillows and beds, and hair and dandruff from domestic pets, though there may be any number of other organic substances such as orris root, pyrethrum, and dusts from flowers, plants, various woods, wickers, and other miscellaneous household articles. When skin reactions are negative in spite of complete testing and retesting, and there is a history of house dust asthma, a complete cleaning of the house after removal of all suspicious furnishings will often give most acceptable relief. When a definite animal emanation reaction is demonstrable by skin testing, the removal of such a substance from the environment is usually effective, though it may be advisable to carry out desensitization to such protein. Desensitization to horse dander protein has been carried out most frequently, though desensitization to cat, rabbit, wool, silk and feather emanation proteins has also been done. Cooke recommends the testing of patients with house dust extracts, especially when the history indicates it and no reactions to organic substances usually found in house dust have been obtained. Though adults have been desensitized to such extracts, we have not found it necessary in any children or in young adults.

Pollen Cases.—Routine testing and retesting with pollens, and a careful analysis of the history from the point of view of pollen allergy, is necessary to uncover this very important factor in the causation of bronchial asthma in children. Pollen treatment must be with antigens made with specific pollens to which the patient is most sensitive, and which are most common in the patient's outdoor environment. For the best results, such treatment should be given preseasonally, although seasonal treatment is nearly always beneficial, especially if the antigen contains the correct pollens. Thus, the preparation of the proper pollen antigen requires complete pollen testing and an accurate knowledge of the botanical flora of the district in which the patient resides.

Orris Root Cases.—Orris root sensitization in this series occurred in only 4.5 per cent., as compared with 10 per cent. in our series of 234 asthmatic subjects of all ages. Removal of all face powder and of the room dust and cosmetics that might contain orris root usually suffices to control the asthma, though desensitization is at times advisable.

Vaccine Therapy.—Vaccine was the sole type of treatment used in four patients in this series of 110 cases, with good results in three of them. Zinsser has shown that bacterial allergy can be produced in animals. It is hard to determine whether bacterial desensitization explains the good results obtained with vaccine in these patients before mentioned. Clinically, however, we feel that bacterial allergy exists, and, accordingly, our rule is to give a small initial dose of 5 or 10 million bacteria to avoid any allergic reaction, increasing the dose according to the skin reaction, but rarely over 500 million is given at one time. Vaccine therapy with both stock and autogenous preparations has been used in all patients with asthma complicated with bronchitis. The favorable results usually are due, in our opinion, to increase in immunity rather than to desensitization. Quartz light therapy has been used in many asthmatic patients with the idea of increasing general resistance. It replaces sun therapy during the greater part of the year. Though it is of great value, asthma is never satisfactorily controlled without treatment based on a correct protein sensitization analysis.

RESULTS

Our treatment of this series of 110 subjects has given complete or nearly complete relief in 68.3 per cent.; marked relief in 22.7 per cent.; slight relief in 6.3 per cent., and no relief in 2.7 per cent. Thus, satisfactory results were obtained in 91 per cent. of this series. The relief obtained has necessitated continued adherence to diet, or to freedom from animal emanation and organic dust contacts, or to desensitization to pollens or other proteins, or finally to combinations of these factors as we have recommended in each case.

CLIMATE

Certain asthmatic patients are relieved by climatic change, especially those living in a high, dry atmosphere. The explanation of such relief may rest in getting away from the specific protein that is causing the asthma, or may be in the resulting dryness of the mucous membranes which makes the absorption of inhalant proteins difficult. However, asthma does develop in such regions, and many asthmatic patients obtain no relief from change of climate. We feel that climatic change for the relief of asthma is no longer necessary. In fact, a few patients whose condition was uncontrolled, whom we sent away for relief, obtained none, and came back to us for further help. Physicians need not advise patients to change climate because of asthma, since such changes may lead to serious financial difficulties, and asthmatic subjects should be controlled in their own communities.

SURGERY

It is recognized by all conservative physicians that operations on the nose and throat rarely cure asthma. Walker, in 1918, advised against such treatment, and many other physicians, including Crowe of Johns Hopkins, have published similar opinions about the control of asthma by surgery. No surgical operations should be performed on asthmatic subjects except for general health, and then seldom before the protein sensitization problem is thoroughly understood and under control. Allergy undoubtedly is responsible for much infection of sinuses and tonsils. Such infection will often improve under proper allergic treatment, and only that which will not so improve or which is acute and endangers life, should be treated with surgery.

CONCLUSIONS

Many disturbances of the respiratory tract in childhood and in young adult life are due to allergy. Asthma occurs frequently during these years and is often mistaken for bronchitis. Careful testing and retesting with a large number of all classes of proteins known to cause asthma has given positive reactions in 95 per cent. in our series of 110 patients. Asthma has been shown to be due to animal emanation, food and pollen proteins in a large percentage of our cases. The importance of pollen sensitization as a cause for asthma in the first two decades of life must be especially emphasized. Surgery on the nose and throat is contraindicated in asthmatic patients, except for the improvement of general health. It is unnecessary to change climate to control asthma. With steady cooperation of the patient, we have obtained satisfactory results in 91 per cent. of this series of asthmatic subjects.

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IS THE DEVELOPMENT OF THE CARPAL CENTERS DELAYED IN RICKETS?*

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During the last few years, a series of papers has been published from this institution on the subject of rickets. They have comprised a consideration of the relative importance of various signs which have been associated for years with rickets, as well as those which have been brought to light more recently, such as the changes in the roentgenograms of the epiphyses and the diminution of the inorganic phosphorus of the blood. The most recent paper of this group was that of Hess and Weinstock,[1] which considers the evolution of the carpal centers from a racial aspect, and which pointed out the fact that negro infants develop carpal centers earlier than do white infants. These authors further confirmed the observation of others to the effect that female infants develop centers somewhat earlier than the males, and drew attention to the high percentage of infants who show carpal centers at the time of birth.

The present report on carpal centers considers the rachitic rather than the normal infant. It is taken for granted in most of the textbooks on rickets, that the rachitic process delays the development of these centers, and indeed that this sign possesses some diagnostic significance. The investigations of this subject are, however, very few and for the most part unconvincing. In many of the clinical phenomena associated with rickets, for example, softening of the ribs,[2] bowing of the legs,[3] craniotabes,[3] delayed dentition, etc., there has been an uncritical acceptance of the validity of this sign. The cases on which this study is based date back to the period when the specific therapy of rickets was not universally accepted and followed. As mentioned in the previous reports, a routine

* Received for publication, Sept. 24, 1925.

* From the Home for Hebrew Infants and the University and Bellevue Hospital Medical College.

1. Hess, A. F., and Weinstock, M.: A Comparison of the Evolution of Carpal Centers in White and Negro New-Born Infants, Am. J. Dis. Child. **29**:347 (March) 1925.

2. Hess, A. F.: Nonrachitic Softening of the Ribs in Infants and Children, Am. J. Dis. Child. **28**:568 (Nov.) 1924.

3. Barenberg, L. H., and Bloomberg, M. W.: The Significance of Craniotabes and Bowing of the Legs, Am. J. Dis. Child. **28**:716 (Dec.) 1924.

examination of infants has been carried out in this institution for the last seven or eight years, in the course of which the various signs and symptoms of rickets have been noted and recorded. The infants on whom this procedure was carried out were under observation for a period of months or years, and it is on the basis of an examination and interpretation of these data that our conclusions are drawn.

The examinations were made at monthly intervals by the same observer, so that the clinical findings are not open to the error of varying subjective interpretation. Throughout our study, the diagnosis of rickets has been based on the accepted criteria, namely, the presence of enlarged costochondral junctions ("beading or rosary"), roentgenologic examinations of the epiphyses, and the estimation of the inorganic phosphate of the blood.

CLINICAL STUDY

So far as we know, there is only one other clinical study [3] which has been fortified by chemical examinations of the blood, and by routine and consecutive roentgenograms. Of approximately 350 children, whose records were complete in regard to roentgenograms and chemical examinations of the blood, we selected, in turn, those in whom carpal centers were absent at the initial examination. We felt it would be unwise to include, in a study of the relation of carpal centers to rickets, infants with centers developed prior to the initial observation, because these centers might or might not have been influenced by rickets. To avoid this possibility, all infants in whom carpal centers were present at the first examination were excluded from the series. Furthermore, the routine method of roentgenographing the wrists at monthly intervals enabled us to observe the earliest appearance of the centers in relation to the development or absence of rickets. The study was limited, therefore, to sixty-two infants. These were divided into two groups: first, infants with rickets, and second, those free from rickets, the latter serving as a control group. Forty infants comprised the rachitic group, and twenty-two the nonrachitic. Their ages at the time of the first examination ranged from 2 to 38 weeks.

The carpal bones are developed from single centers, and make their appearance generally shortly after birth in the os capitatum (magnum) and unciform bones as cartilaginous centers. Roentgenographically, they appear in the normal infant as shadows, round or oval in shape, and are sometimes seen to be composed of several small nuclei. Although it is not uncommon to find carpal centers at birth, this is not the rule; the time of their appearance in postnatal life is subject to marked variation.

Twenty-two of the forty infants with rickets (or 55 per cent.) developed their first carpal centers during the first 6 months of life, whereas sixteen (or 40 per cent.) did not manifest a center until after the

first half year (Table 1). Two of these sixteen infants (aged 7 and 12 months, respectively) failed to develop a center after an observation of seven and twelve months, respectively. Four infants developed a center at three months; in another with marked rickets, this was delayed until the fourteenth month. Of the forty infants with rickets, five (or 12.5 per cent.) developed second or subsequent centers (following the appearance of the first) between the third and sixth month; fifteen (or 37.5 per cent.) developed them between the seventh and eighteenth month, and twenty (or 50 per cent.) did not show subsequent centers within a period of from four to fourteen months of observation. Only one infant with rickets showed a third carpal center, which appeared at 11 months, although some of the infants were observed for eighteen

TABLE 1.—*Infants with Rickets. Age When Carpal Centers First Appeared*

	Number of Infants with				
	First Centers		Subsequent Centers		
Age, Months	1	2	2	3	Radial
1	0	0	0	..	..
2	0	0	0	..	..
3	4	0	0	..	..
4	2	4	0	..	..
5	5	4	3	..	..
6	1	2	2	..	..
7	3	1	5	..	..
8	1	0	0	..	..
9	0	5	1	..	1
10	1	1	0	..	0
11	3	0	0	1	1
12	0	0	0	..	1
13	0	0	0	..	0
14	1	0	1	..	2
15	..	0	0	..	0
16	..	0	1	..	1
Total*	21	17	13	1	6

* Two infants (aged 7 and 12 months, respectively) did not develop centers during seven and twelve months observation.

months. Six of the infants with rickets did not show radial centers until the ninth to the sixteenth month.

Eighteen of the twenty-two infants without rickets (or 82 per cent.) developed carpal centers within the first 6 months of life, and four had centers at 8 and 9 months (Table 2). One of these developed two centers at 1 month of age. Seven of the twenty-two free from rickets (or 32 per cent.) developed second or subsequent centers within the first 6 months (see chart); two developed a third center, one at 6 months and one at 8 months; one had a radial center as early as the sixth month.

One of the most constant roentgenographic findings in rickets is a greater or less degree of rarefaction of bone. The presence of carpal centers roentgenographically, therefore, must depend on the existence of

calcium in those cartilages. Since uncalcified areas give negative shadows, we should expect a delay in the evolution of carpal centers, and a comparative lack of them in rickets. Our findings (Tables 1 and 2 and the chart) lead to the conclusion that in rachitic infants the evolution of carpal centers is delayed, compared to normal infants.

Plaut [4] also found an actual delay in the appearance of the carpal centers in rickets. This agrees with our observations. The calcification centers have been shown to be present histologically, but are not manifest by roentgenogram because of the lack of calcification.[5]

Pryor [6] and Stettner [7] state that the development of first center for normal infants is between the third and the sixth month for the female, and between the fourth and the tenth month for the male. In our group of infants with rickets, there were twenty-five boys and fifteen girls;

TABLE 2.—*Infants Without Rickets. Age When Carpal Centers first Appeared*

	Number of Infants with				
	First Centers		Subsequent Centers		
Age, Months	1	2	2	3	Radial
1	0	1	0	..	..
2	3	2	0	..	..
3	0	2	2	..	..
4	2	2	0	..	..
5	2	2	1	..	..
6	1	1	2	1	1
7	0	0	1	..	..
8	0	2	1	1	..
9	1	1	0	..	..
10	..	..	1	..	..
11	..	..	1	..	..
12	..	..	..	..	..
13	..	..	..	..	1
14	..	..	..	..	..
15	..	..	..	..	..
16	..	..	..	..	..
17	..	..	..	..	..
18	..	..	..	..	2
Total	9	13	9	2	4

in the group without rickets, there were fifteen boys and seven girls. As the male sex tends to delay the period at which the carpal centers appear, the nonrachitic group, composed two-thirds of males, should have shown an increased delay in the appearance of carpal centers. As a matter of fact, the reverse was found.

We agree with Plaut [4] that decalcified areas leave negative shadows, but disagree with his statement that "in the florid stage of rickets new

4. Plaut, H. F.: Roentgenuntersuchugen über die Knochenkernbildung bei Rachitis, Ztschr. f. Kinderh. **38**:540 (Aug.) 1924.

5. Wimberger, H.: A Study of Developing Florid and Healing Rickets as Demonstrated by X-Ray Photography, Part III, No. 1, p. 95, Medical Research Council, London, Studies of Rickets in Vienna, 1919-1922.

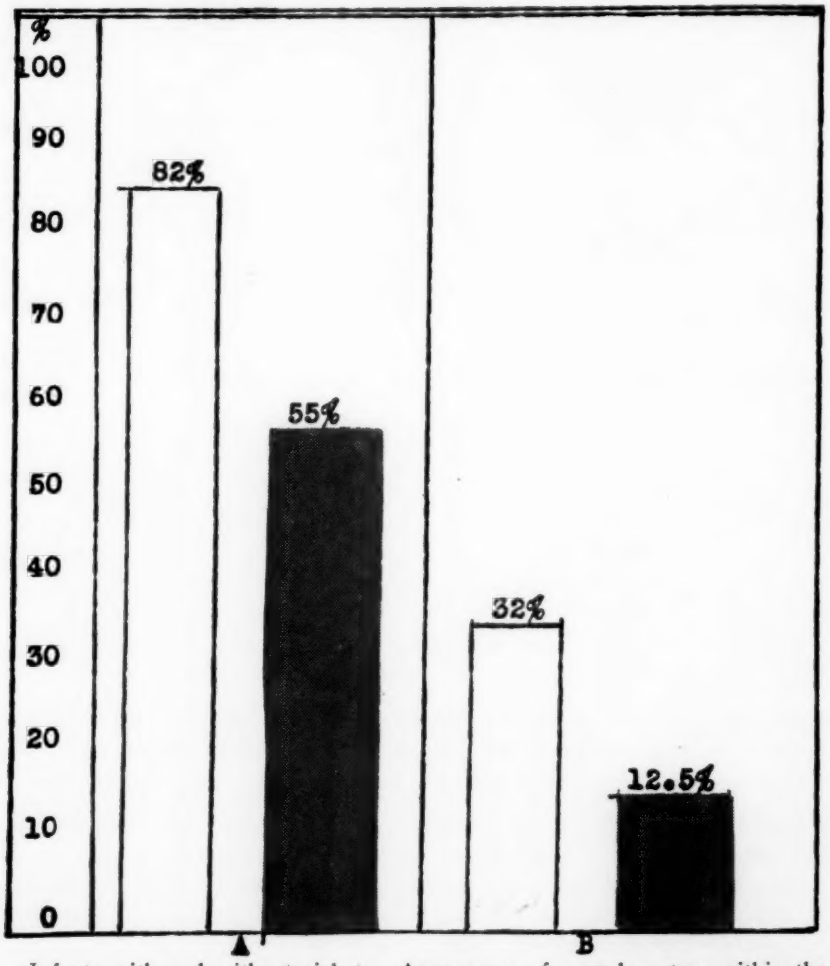
6. Pryor, J. W.: Bull. State College of Kentucky, 1906; Bull. Univ. of Kentucky, 1908.

7. Stettner, E.: Arch. f. Kinderh. **68**:742 (Dec.) 1920.

calcification centers do not appear by roentgenograph." Although delayed, thirty-three of the forty infants with definite rickets (or 82 per cent.) showed new carpal centers during the active stage of the disease.

ANTIRACHITIC THERAPY

Numerous investigations have been made to determine the effect of antirachitic therapy on the signs and symptoms of rickets, but little or



Infants with and without rickets. Appearance of carpal centers within the first 6 months. *A*, appearance of first carpal centers; *B*, appearance of subsequent centers. Normal infants, white columns; rachitic infants, black columns.

no studies have been carried out to ascertain the effect of such specific treatment on the development of carpal centers. Twenty-five infants with rickets received antirachitic therapy, varying in duration from one

to eight months. Of these, only five developed centers within a period of two months. The antirachitic measures consisted of yolk of egg, cod liver oil, ultraviolet rays (mercury quartz light and carbon arc) and sunlight.

The changes observed in the epiphyseal centers of ossification in rickets are similar to those in the shafts of the long bones. The density of the shadow is decreased evenly throughout, and in the very severe cases rarefaction is so pronounced that the center appears completely washed or punched out—an empty body often mistaken for an artefact, a ring which has lost its normal sharp outline. In severe rickets, centers which were previously visible may become invisible as a result of the calcium poverty. This phenomenon was observed in two instances.

When healing begins, it proceeds rapidly and is attended by a restoration of the process of calcium deposition. Roentgenographically, the change is seen by a sharper demarcation between bones and soft tissue due to a calcification of the cortex, and an increasing intensity of the shadow. The more vigorous the tendency to heal, the quicker does the intensity and size of the shadow increase. The most definite indication of calcification is the appearance of a finely etched periosteal margin, sharply distinguished from the shadow of the ossification center itself.

SUMMARY AND CONCLUSIONS

1. The appearance of carpal centers in infants with rickets was later than in infants free from rickets. Twenty-two of the forty infants with rickets (or 55 per cent.) developed their first center during the first 6 months of age, whereas eighteen of the twenty-two infants free from rickets (or 82 per cent.) developed carpal centers during a corresponding period.

2. The development of second or subsequent carpal centers in infants with rickets was delayed, compared to their appearance when rickets was absent. Five of the infants with rickets (or 12.5 per cent.) developed second or subsequent carpal centers within the first 6 months of life, whereas seven of the infants free from rickets (or 32 per cent.) developed them during the corresponding period.

3. The development of more than two carpal centers during the first 6 months of life was retarded in rachitic infants compared to non-rachitic infants. None of the infants with rickets had more than two carpal centers, whereas two of those free from rickets had three carpal centers or a radial center.

4. Although delayed, new calcification centers appeared during the active stages of rickets. Thirty-three (or 82 per cent.) of the infants

with rickets showed new calcification centers during the active stages of the disease.

5. Antirachitic treatment (cod liver oil, ultraviolet rays or yolk of egg) rarely brought about a development of carpal centers within a period of two months.

2562 Grand Concourse.

BLOOD CHEMICAL FINDINGS DURING CONVULSIONS IN ACUTE HEMORRHAGIC NEPHRITIS

REPORT OF CASE *

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An investigation of the blood chemistry during convulsions in nephritis has not been noted in a search of the recent literature. In the case reported here, not only a series of blood studies during convulsions, but also a correlation of the blood chemical findings preceding and subsequent to these attacks are presented. The outstanding features of this study are the changes which the convulsions induced in the sugar and the alkaline reserve, as well as the absence of marked changes in the other blood constituents investigated.

REPORT OF CASE

History.—The patient, a boy, aged 7 years, had no history of illness other than occasional mild colds with sore throat. His family and past history were unimportant. Except for the fact that during the month prior to admission to hospital, the child's appetite had been poor and he had frequently complained of headaches, his present illness dates from one week before entry. While attending school, he was suddenly seized with a severe epigastric pain, accompanied by headache and vomiting. For a period of four days he vomited practically all solids and fluids taken. The second day following the onset of illness, his eyes were almost closed by edema of the lids. The hands and ankles also showed a rapidly developing edema, and on this day, for the first time, the urine contained a considerable amount of blood. He appeared drowsy from the onset, but did not complain. Previous to this illness he had had nocturia only occasionally, but this was now increased to three and four times, with no further urinary symptoms.

At the time of entrance to the hospital, the patient had an elevation of temperature to 102 F.; there was also moderate edema of the eyelids, legs and ankles. The skin was pale, dry and waxy in appearance. The breath was slightly uriniferous, and the throat was found to be reddened, with the tonsils moderately hypertrophied. The dental hygiene was fair. A slight general adenopathy was present, with markedly enlarged submaxillary glands. The heart was negative except for a soft systolic murmur at the apex. The abdomen was moderately distended but otherwise it was normal. There was a slight costovertebral tenderness on palpation, which was more marked on the right side. The reflexes were generally hypoactive and no kneejerks could be elicited. The blood pressure on entry was 118 systolic, 78 diastolic. Urinalysis showed a slight trace of albumin, numerous red and white blood cells, and a number of fine granular casts. Otherwise, the general routine laboratory tests

* Received for publication, Oct. 5, 1925.

* From the Children's Medical Service, Massachusetts General Hospital, under the direction of Dr. Fritz B. Talbot.

were negative, except for nonprotein nitrogen of 98 mg. per hundred cubic centimeters of blood on entrance to the hospital. On the basis of these data, a diagnosis of acute hemorrhagic nephritis was made.

The patient was confined to bed and was given a diet low in protein and salt. The fluid intake was limited to 1,500 c.c., which was later increased to 2,400 c.c. Two weeks after entry there was a definite improvement in the boy's general appearance, the edema having subsided. During the last week there had been no further vomiting but the boy had an occasional mild epistaxis. Although his blood pressure had increased to 160 systolic, 100 diastolic, his temperature remained only from 1 to 2 degrees above normal, and his pulse and respirations were practically normal. The urine still showed a slight trace of albumin, many red and white blood cells, and occasional granular casts. A urine culture gave no growth.

Blood Chemical Studies in Relation to Convulsions

Time Blood Taken	Nonprotein Nitrogen, Mg. per 100 C.c.	Uric Acid, Mg. per 100 C.c.	Blood Sugar, Mg. per 100 C.c.	Plasma Sugar, Mg. per 100 C.c.	Spinal Fluid Sugar, Mg. per 100 C.c.	Carbon Dioxid, Percentage by Volume	*p*H	Plasma: Phosphorus, Mg. per 100 C.c.	Plasma: Calcium, Mg. per 100 C.c.	Plasma: Chlorid, Mg. per 100 C.c.
Normals.....	20-30	3-4	80-100		55-75	50-60	7.32-7.41	2.5-4	9-12	580-640
11/21/24.....	98	..	..	..	..	..	..	..	..	..
12/ 6/24.....	27	8.16	.	..	..	47	7.41	7.4	..	..
12/10/24.....	58	..	..	..	..	..	..	..	..	..
12/11/24.....(Duration of convulsion: 8:00 a. m. to 10:30 a. m.)										
9:00 a. m.*†	**49**	**4.32**	**312**	..	..	**21**	..	..	..	..
1:30 p. m.*	**32**	**6.48**	**200**	..	..	**40**	**7.21**	**6.6**	**10.2**	..
3.50 p. m.*	**64**(Pl.)	..	..	**122**	**136**	..	..	..	..	**621**
12/13/24.....	71	4.98	75	..	..	40.5	..	7.1	..	..
12/15/24.....	41	2.52	110	..	..	41.2	..	..	..	..
12/19/24.....(Duration of convulsions: 5:50 p. m. to 8:10 p. m.)										
6:03 p. m.*†	**49**	**4.84**	**174**	..	..	**45.2**	..	**7.8**	..	..
8:05 p. m.*†	**38**	**4.6**	**291**	**319**	**107**	**36.3**	..	**7.8**	..	**603**
11:10 p. m.*.	**37**	**4.76**	**179**	..	..	..	..	..	..	..
12/20/24										
9:35 a. m...	40	4.88	89	..	..	..	..	..	..	..
1/ 9/25.....	59	3.84	91	..	..	37.5	..	..	..	658
1/14/25.....	45	3.72	77	..	..	44.7	7.43	..	..	643
1/30/25*†.....	**59.4**	**6.44**	**250**	..	..	**41.2**	..	**9.1**	..	..
2/ 5/25.....	76.8	5.12	103	..	..	29.0	..	16.8	..	..

* Convulsive periods in heavy print.
† Convulsions.

A chemical examination of the blood was made on December 6, about one week before his first series of convulsions; this examination was approximately normal except for a high phosphorus content of 7.4 mg. per hundred cubic centimeters of blood plasma.[1]

The blood chemistry was studied during three series of convulsions. Three determinations were made during his initial convulsions on December 11, several weeks after entry. During his next spasmodic attack the following week (December 19), three specimens of blood were also obtained. The last blood examination during the convulsions was made (January 30) much later in the

1. Briggs, A. P.: Some Applications of the Colormetric Phosphate Method, J. Biol. Chem. **59**:255 (March) 1924.

course of his illness, at a time when he was having very frequent seizures and when his general condition did not warrant the withdrawal of more than one sample of blood.

Up to the night preceding his initial convulsions, the patient's general condition and his clinical symptoms had definitely improved without further change in the treatment. That evening, he suddenly complained of a severe headache which was followed by vomiting twice during the night. The next morning, December 11, at 8:00, he was dull and unresponsive and shortly afterward, for the first time, developed a severe generalized convulsion which last almost continually for two and a half hours, and was finally relieved by paraldehyd (3 c.c., given per rectum). During the convulsion, the temperature rose to 103.5 F., and the patient perspired profusely. His general pallor was accentuated by the contrast with his lips, which were cherry red in color. The breath suggested the sweet fruity odor of acetone, and a less pronounced uriniferous odor. Ophthalmoscopic examination revealed no pathologic changes of the eyegrounds.

The first sample of blood taken at 9:00 a. m., an hour after the onset, and during the height of the initial convulsion, had a nonprotein nitrogen[2] content of 49 mg. per hundred cubic centimeters of blood, which was a drop from 58 mg. per hundred cubic centimeters of blood found on the previous day. The carbon dioxid combining power was very low, only 21 per cent. by volume, thus indicating a severe acidosis. The most surprising finding was a blood sugar[3] content of 312 mg. per hundred cubic centimeters of blood.

Three hours after the convulsion, while the patient was in a semicomatose condition, another specimen of blood was withdrawn (1:30 p. m.). The uric acid[4] had risen to 6.48 mg. per hundred cubic centimeters of blood. The carbon dioxid combining power[5] had reached the more normal value of 40 per cent. by volume. The p_H of the blood, at this time, showed that despite the increased alkaline reserve (as shown by the carbon dioxid combining power) there was still a marked acidosis (p_H 7.21).[6] The phosphorus was elevated and the calcium was normal. The sugar had fallen to 200 mg. per hundred cubic centimeters of blood, which was still quite high.

Two hours later, the sugar content of the blood plasma had fallen to an approximately normal level, while the sugar content of the spinal fluid was greatly in excess of the average value, and slightly higher than that of the blood plasma drawn simultaneously. The urine obtained immediately afterward was free from sugar, acetone and diacetic acid, but albumin, red and white blood cells, and granular casts still persisted.

On December 15, a sample of blood was taken because the patient refused lunch, complained of a headache and vomited profusely. Although another series of convulsions was feared, none occurred, and there was an improvement in his symptoms in the course of the next few days. At this time the boy had no edema except for a puffiness of the eyelids.

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2. Folin, O., and Wu, H.: System of Blood Analysis, J. Biol. Chem. **38**:81 (May) 1919.

3. Folin, O., and Wu, H.: System of Blood Analysis — Simplified and Improved Method for the Determination of Blood Sugar, J. Biol. Chem. **41**: 367 (March) 1920.

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5. Van Slyke, D. D.: Studies of Acidosis. II. A Method for the Determination of Carbon Dioxid and Carbonates in Solution with Modifications, J. Biol. Chem. **30**:347 (June) 1917.

6. Cullen, G. E.: Studies of Acidosis. Colorimeteric Determinations of Hydrogen-Ion Concentration of Blood Plasma, J. Biol. Chem. **52**:501 (June) 1922.

On the afternoon of December 19, however, he again began to vomit. His blood pressure had risen to 170 systolic, 80 diastolic. Twitchings were observed around the corners of his mouth, but were not definitely convulsive in character. Twenty grains of sodium bicarbonate were given orally. An hour later he started to have a number of severe convulsions, and a sample of blood taken immediately showed among other findings a sugar content of 174 mg. per hundred cubic centimeters of blood. The first two specimens of blood in this group were obtained at the height of the convulsions, and the third when the child had been semicomatose for some time. Two hours after the onset of attacks, a lumbar puncture was made during a very severe convulsion, and a clear spinal fluid[7] was obtained under considerably increased pressure. Within a few minutes a second specimen of blood was withdrawn. The whole blood sugar had risen to 291 mg. per hundred cubic centimeters of blood; plasma sugar was 319 mg. per hundred cubic centimeters of blood, and the spinal fluid sugar was 107 mg. per hundred cubic centimeters of spinal fluid. Following the lumbar puncture and the withdrawal of blood, 4 c.c. of paraldehyd was given per rectum, and later 20 grains of soda bicarbonate was given by nasal tube. The patient then became quiet and remained in a semicomatose state all night. The blood sugar in a third sample, collected while the patient was still in this condition, five hours after the start of convulsions, was found to have fallen to 174 mg. per hundred cubic centimeters of blood. The next morning the blood sugar had returned to normal.

	Dec. 11	Dec. 19
Total protein	26	17
Spinal fluid sugar	136	107
Spinal fluid nonprotein nitrogen	43	
Spinal fluid chlorid	749	743
Gold colloidal test	4454321100	1225321100
Initial pressure	210	260

The last chemical study during a convulsion was made on the sample of blood taken January 30. The progressive course of the disease at this time probably accounts for the increase in the nonprotein nitrogen, uric acid and phosphates, while the high sugar may be attributed to the attack itself.

For some time after the first two series of convulsive seizures, despite the fact that the patient was brighter and more responsive, the urinary findings and the high blood pressure continued, indicating that the nephritis had become chronic. Early in January, the edema had greatly increased involving the abdomen and genitalia, and persisted constantly for the next month until practically a general anasarca had developed. The patient had frequent vomiting attacks, and convulsions recurred at irregular intervals. The blood findings during this latter period, corresponded, in general, to those previously obtained.

Various types of therapy, including sodium bicarbonate, calcium chlorid and intravenous magnesium sulphate, were instituted during the course of the stay in the hospital, none of which proved of any curative value in this case. The boy continued to become progressively worse, finally developing anuria, Cheynes-Stokes breathing and coma terminating in death.

COMMENT

Carbohydrate metabolism is said to be disturbed in some cases of nephritis.[8] In fact, in the early stages of interstitial parenchymatous

7. Spinal fluid examination (Neurological Lab. M. B. H.), supplied by Dr. F. Fremont-Smith.

8. Hoobler, R. B.: Nephritis, Abts Pediatrics **4**:907, 1924.

nephritis, the blood sugar has at times been reported as very high, equaling that found in severe diabetes. Since observations on this patient before the convulsive attacks indicated that the usual level of the blood sugar was within normal limits, the increased sugar content must be attributed to the convulsive seizures rather than to the nephritis per se. This rise in blood sugar may have been simply a result of a severe generalized disturbance of the whole system, with an increased epinephrin output and subsequent mobilization of the sugar.

A comparison of the series of blood findings on the two days when very severe convulsions occurred, namely, December 11 and 19, revealed a most interesting observation in the similar rise of the blood sugar during convulsions and the subsequent fall with the cessation of attacks. It was also of interest to note on December 11 not only a rise of the spinal fluid sugar, but also that it was of a higher value than the blood plasma taken simultaneously when the sugar content of the blood was found to be decreasing. This would seem to indicate a slower return to normal of the spinal fluid than of the blood.[9] On December 19, when the blood sugar was increasing, the increase of sugar in the plasma was greater than that in the whole blood. Although the spinal sugar rose to a much higher level than normal, its increase was apparently delayed as compared to either the plasma or to the whole blood. From this one case studied, it might be deduced that there is a slower fluctuation of sugar in the spinal fluid than in the blood.

In the first series of convulsions, the carbon dioxid combining power of 21 per cent. by volume was even lower than would have been expected from the marked clinical symptoms. The rise in three and a half hours to 40 per cent. by volume, was during the time when convulsions were much less severe, although there was still a severe acidosis, as indicated by the p_H of 7.21. In the second series of convulsions, on December 19, both determinations of carbon dioxid combining power were of a more normal value than those recorded in the initial convulsions; however, in this series, previous to the drawing of any blood, sodium bicarbonate had been given orally in small amounts. In the last convulsions chemically studied, January 30, the carbon dioxid combining power was 41.2 per cent. by volume, the blood having been procured early in the attack. The patient had been receiving 30 grains of sodium bicarbonate orally three times daily for three days. The low finding of 21 per cent. by volume in the first series of convulsions may be due merely to violent activity, which, if sufficient, causes an acidosis indicated both by the p_H and by the carbon dioxid combining

9. Polonovski, M., and Duhot, E.: Sugar in Blood and Spinal Fluid, Presse méd. **31**:60 (Jan.) 1923.

power.[10] On the other hand, the low carbon dioxid combining power, February 5, when there were no convulsions, was presumably not due to activity but to a retention acidosis, as further evidenced by the accumulation of phosphates.

The phosphorus was elevated throughout the whole course of the disease, and was not affected by the convulsions. The two values obtained during the second series were identical (7.8), which finding does not differ greatly from an earlier determination (7.4), at a time when there had been no convulsions. The last blood phosphate recorded (February 5) was 16.8 mg. per hundred cubic centimeters of blood plasma. It, therefore, would seem that the high blood phosphorus is rather a nephritic than a convulsive variable. There is often a retention of phosphorus in the blood in nephritis, but fatal cases show a rapid terminal increase in plasma phosphates.[11]

Single plasma chloride determinations during the first and second series of convulsions gave findings within normal limits.

The nonprotein nitrogen remained moderately high throughout the greater part of the boy's illness. There was no appreciable change during convulsions, except that the level was slightly higher at their onset than immediately afterward, when the nonprotein nitrogen was approximately normal.

The uric acid showed no consistent change during the convulsive periods, except in two instances when there was a higher value than in any of the nonconvulsive periods. However, in the second series of attacks, the more detailed studies of the uric acid showed no change in relation to convulsions. For this reason, no conclusion can be drawn as to the significance of the high uric acid findings.

From a general survey of the before-mentioned chemical studies, it is of special interest to note that the greatest changes which occurred during the convulsions were in the sugar and the carbon dioxid combining power, two blood constituents which usually do not vary greatly in the average case of nephritis. On the other hand, the nonprotein nitrogen and the phosphorus, in which there is often a high value attributable to a nephritic etiology, were not further affected by the convulsions to any appreciable extent.

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10. Barr, D. P.; Hunwich, H. E., and Green, R. P.: Studies in the Physiology of Muscular Exercise. Changes in Acid-Base Equilibrium Following Short Periods of Vigorous Muscular Exercise, J. Biol. Chem. **55**:495 (March) 1923. Shaw, E. B., and Moriarty, M.: Hypoglycemia and Acidosis in Fasting Children with Idiopathic Epilepsy, Am. J. Dis. Child. **28**:562 (Nov.) 1924.

11. Denis, W., and Minot, A.: Study of Phosphate Retention from Standpoint of Blood Analysis, Arch. Int. Med. **26**:99 (July) 1920.

CONCLUSIONS

Convulsions in a child with acute hemorrhagic nephritis resulted in the following changes in the chemistry of the blood:

1. The sugar content of the blood was greatly increased, a phenomenon which occurred more slowly in the spinal fluid. There was a rapid return of the blood sugar to normal following the convulsions, and a delayed fall of the spinal fluid sugar.

2. The alkaline reserve decreased during convulsions (when no alkaline therapy was given).

3. The phosphorus was unaffected by the convulsions, the constantly high value being attributed to the nephritis.

4. The moderately elevated nonprotein nitrogen, due to the nephritis, was further unchanged except for a slight decrease following the convulsions.

5. No definite change was found in the plasma chlorids or in the uric acid during convulsions.

DIPHTHERIA FOLLOWING TONSILLECTOMY

LOCAL RESISTANCE AND GENERAL IMMUNITY TO DIPHTHERIA *

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The serious nature of diphtheria as a complication following tonsillectomy is due to the fact that the disease is likely to be overlooked until it is almost too late for antitoxin administration. Most of the mischief that can possibly result from the absorption of the toxin will probably already have taken place before the operator suddenly realizes that he has a fatal diphtheritic intoxication to deal with. The postoperative sloughing membrane following the removal of the tonsils closely resembles a diphtheritic pseudomembrane, and is, therefore, a source of great danger in overlooking the superimposed secondary diphtheria. The purpose of this paper is to emphasize this danger, to indicate the necessity of taking nose and throat cultures before operations on these structures, and to protect positive diphtheria carriers by a prophylactic dose of antitoxin. This precaution, of course, would not be necessary if the patient to be operated on had been tested previously for diphtheria immunity and gave a negative Schick test. Moreover, within a week or two after the operation, should diphtheria bacilli lodge within the nasopharyngeal passages of the patient, such an immunity, indicated by a negative Schick test, would protect him against superimposed local infection and constitutional intoxication.

Within the last three months, four patients have been brought to my attention, in whom a diphtheritic lesion of the fauces developed immediately after tonsillectomy. One child was seen in private practice; the other three were seen at the Willard Parker Hospital. Of the four, one of the hospital patients died within twenty-four hours after admission; the other three were saved at the eleventh hour by recognition of the disease, although all of them developed a diphtheritic paralysis of the palate, and in one patient convalescence was complicated by an attack of aspiration pneumonia.

REPORT OF CASES

Case 1.—P. S., a boy, aged 3 years, had his tonsils and adenoids removed April 21, 1925. On April 27, six days after the operation, I saw the patient for the first time. An extensive exudate was present, covering both tonsillar

* Received for publication, Sept. 24, 1925.

regions and extending over the pillars of the fauces, uvula and entire visible portion of the posterior pharyngeal wall. The uvula was edematous, the size of the small finger. Without waiting for any culture report, I injected the child with 10,000 units of antitoxin intramuscularly. The cultures from the nose and throat proved positive for virulent diphtheria bacilli. Five weeks after the tonsillectomy, the patient developed paralysis of the palate with nasal voice and escape of fluids through the nose. These symptoms gradually cleared up, and the patient made a complete recovery.

In connection with this case, it is interesting to note that the two older sisters of the patient had been injected with diphtheria toxin-antitoxin four years prior to this. When retested with the Schick test during their brother's illness, they gave a negative Schick reaction and were, therefore, still immune to diphtheria.

CASE 2.—A. H., a girl, aged 4 years, was admitted to the hospital, June 29, 1925. Her tonsils had been removed five days previously. On admission the child appeared toxic, cyanoic, and had a temperature of 104 F. Examination showed an exudate covering both tonsillar fossae, extending over the pillars and over the edematous uvula. The cervical glands were enlarged on both sides. The child had a croupy cough, no stridor, but had slight retraction of the chest. Direct laryngoscopic examination showed visible exudate on arytenoids and false vocal cords, extending below the true vocal cords. By means of suction, several pieces of membrane were removed from the larynx, resulting in temporary relief. The throat and nose cultures were positive for diphtheria bacilli. Ten thousand units of antitoxin were injected before admission and 9,000 units were given intravenously after admission. The general condition became rapidly worse, however, and the patient died the following day.

CASE 3.—M. T., aged 9 years, was admitted to the hospital, July 11, 1925. The patient was a diphtheria bacillus carrier, on whom a tonsillectomy had been performed eleven days (June 30) previous to admission to the Willard Parker Hospital. Seven days after the operation, the membrane over the tonsillar fossae began to spread over the uvula and the soft palate. The patient was reported to have received 15,000 units of antitoxin on that day. On admission four days later, examination of the throat showed a membranous exudate covering pillars, soft palate and both sides of the edematous uvula. The throat cultures were positive for diphtheria bacilli. Nine thousand units of antitoxin were injected. Six days after admission to the hospital, the patient showed signs of pulmonary consolidation in the right upper lobe, probably resulting from aspiration following the tonsillectomy. Paralysis of the palate developed on July 19, nineteen days after the operation. The patient gradually improved and made a complete recovery.

This case is of special significance because of the frequency with which carriers of diphtheria bacilli have been treated recently by tonsillectomy. The only justifiable procedure to follow in such cases is to make certain that these patients show a negative Schick test before the operation, or that they receive a prophylactic dose of 1,500 units of antitoxin.

CASE 4.—F. E., aged 3 years, had had an attack of scarlet fever and diphtheria in November, 1924. Tonsillectomy was performed July 8, 1925. Three weeks later (July 29), the child became croupy, and was admitted to Willard Parker Hospital August 5, twenty-eight days after the operation. The throat examination showed membranous exudate over both tonsillar fossae, pillars and sides of the uvula. There was moderate enlargement of the anterior cervical glands. The temperature on admission was 103 F. Nine thousand units of diphtheria antitoxin were injected intravenously and 20,000 units intramuscularly. Direct laryngoscopic examination showed exudate on the ventricular border and epiglottis, with marked local edema. Intubation was performed the day after the patient was admitted to hospital. The throat and nose cultures were positive for diphtheria bacilli. Paralysis of the soft palate

and escape of fluids through the nose appeared August 13, eight days after admission to the hospital and fifteen days after onset of illness. Palatal paralysis gradually cleared up, and the patient recovered.

The time of the appearance of the diphtheria infection after the tonsillectomy is of interest in this case. The bacilli probably lodged in the throat after the operation, while in the first three cases the organisms must have been present in the nasopharyngeal passages at the time the tonsils were removed.

COMMENT

Diphtheria is likely to develop in a patient who has just been operated on for tonsillectomy and adenoidectomy, if the person is susceptible, as can be shown by a positive Schick test, and if he is a carrier of virulent diphtheria bacilli. While these three factors—absence of general immunity to diphtheria, presence of virulent diphtheria bacilli in the nose or throat and an operation, such as tonsillectomy—may not come together frequently, yet when they are present in the same person, diphtheria is quite certain to follow and the disease is likely to prove very dangerous, possibly fatal. The serious nature of the superimposed diphtheria arises from the danger of an early and rapid absorption of a fatal dose of toxin from the extensive raw surface, and the difficulty of recognizing the disease in the sloughing postoperative membrane until much valuable time has been lost and the opportunity for effective administration of antitoxin has slipped by.

Diphtheria may also readily develop as a result of a superimposed infection with diphtheria bacilli occuring in a susceptible person from one to two weeks after an operation on the tonsils and adenoids. At this time, the wound has not yet completely healed, and the resistance of the mucous membrane to infection is still below normal. Such conditions show how necessary it is that patients who are to be operated on for nose and throat conditions should be constitutionally immune to diphtheria, irrespective of whether the throat cultures taken before the operation are positive or negative for the Klebs-Loeffler bacillus. To accomplish this, general immunization of all young children with toxin-antitoxin or with toxoid would be a very desirable procedure.

It is interesting at this point to consider the relation between local resistance to infection inherent in the normal mucous membrane and the general antitoxic immunity, known as "natural" immunity to diphtheria. Such immunity can be demonstrated by a negative Schick test. A person may be susceptible to diphtheria, show a positive Schick test, and yet may be a temporary carrier of virulent bacilli without actually developing the disease. An operative procedure on the throat, such as removal of tonsils and adenoids, or an acute infectious process, such as a cold or an attack of scarlet fever, may diminish or destroy the local resistance inherent in the normal mucous membrane, and the patient

will then be more than likely to develop clinical diphtheria with constitutional symptoms of intoxication.

We do not yet know definitely the nature of the local resistance of the intact normal mucous membrane which can successfully protect a susceptible carrier against local infection with a pathogenic organism and constitutional intoxication with its products, such as the diphtheria bacillus and its toxin. Clinical observations are sufficiently frequent, however, to indicate that such local protection does exist.

Local resistance of the intact normal mucous membrane is present not only for diphtheria but also for scarlet fever infection. Such resistance may be seen in the following cases. A child was admitted to the scarlet fever pavilion, with the diagnosis of scarlet fever, but this was not corroborated by the result of the Dick test. The latter was strongly positive each time the child was tested. Although the patient evidently had no general antitoxic immunity to scarlet fever and was fully exposed to infection in the ward, yet she did not develop the disease until the twenty-seventh day after admission. Three days before the attack of scarlet fever, this patient developed chickenpox, which evidently by breaking down the local resistance of the mucous membrane was the indirect cause for the attack of scarlet fever that promptly followed. Another case will illustrate the effect of diphtheria in breaking down the local resistance to infection with scarlet fever. One of the assistant resident physicians at the Willard Parker Hospital remained on service in the scarlet fever pavilion for three months without developing the disease. This promptly occurred, however, after the physician was placed in charge of the diphtheria pavilion, when he contracted tonsillar diphtheria. The scarlatinal streptococcus was probably present in his throat passages, but was harmless for the time being until the attack of diphtheria destroyed the local resistance of the mucous membrane to infection with this pathogenic organism.

SUMMARY AND CONCLUSION

1. It is strongly advisable that preliminary nose and throat cultures for diphtheria bacilli be taken as a routine before such operations as tonsillectomy and adenoidectomy. If the cultures are positive, a prophylactic dose of 1,500 units of diphtheria antitoxin should be injected, unless the patient has already been tested with the Schick test and shows a definite negative or a negative pseudoreaction.

2. In carriers who are to be treated by the removal of tonsils and adenoids, it is especially important to make certain that the patient either gives a negative Schick reaction or, if a positive Schick reaction is obtained, that he receives a prophylactic dose of diphtheria antitoxin.

3. Infection with the diphtheria bacillus and development of the disease clinically may occur a week or two after tonsillectomy, and before the operative wound has completely healed. Preliminary throat cultures in these cases would be negative for the Klebs-Loeffler bacillus.

4. The best safeguard against diphtheria as an operative complication in nose and throat surgery would be active immunization of all young children with the new one-tenth L + mixture of toxin-antitoxin or with diphtheria toxoid. The antitoxin immunity thus established would protect the person to be operated on against local infection with the diphtheria organism and systemic intoxication with its toxin.

5. The intact normal mucous membrane of the nasopharyngeal passages has a definite local resistance which protects persons, who have no general antitoxic or antibacterial immunity, against the action of such pathogenic bacteria as the diphtheria and scarlet fever organisms and their toxins. The nature of this local resistance is not yet definitely known. It may readily be destroyed by an operative procedure such as tonsillectomy, or by an inflammatory process such as a cold, an attack of scarlet fever or of diphtheria.

6. It follows that the periods of incubation, as usually understood by general practitioners and health officers, hold good only under conditions in which the infecting organism or virus is highly virulent for the human race, and in which the normal mucous membrane presents no barrier to invasion. This is the case with measles, in which disease the period of incubation is quite definite. With other diseases, such as diphtheria and scarlet fever, which are not so highly infectious for man, the period of incubation depends to a greater extent on the interplay of factors, such as the local resistance of the mucous membrane, the variable virulence of the infectious agent and the general specific resistance of the individual. The periods of incubation in these two diseases may be extended, the final development of the disease in a susceptible person depending on some factor such as trauma or infection, which destroys the local resistance of the intact mucous membrane and with it the nonspecific protection of the patient.

WHEAL FORMATION IN INFANTS AND IN CHILDREN

I. IN EDEMA, CRETINISM, SCLEREDEMA, SCLEREMA, NEPHRITIS, CARDIAC DISEASE, SEVERE PROSTRATION AND TUBERCULIN POSITIVE SUBJECTS *

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The phenomenon of wheal formation (urticaria) of the skin is dependent on certain vascular phenomena, namely, dilation of the vessels and increased permeability of vessel walls, resulting in localized edema of the skin. As it has been observed that wheal formation is modified in a measureable degree in cardiac edema,[1] it seemed advisable to study it in other conditions. It was hoped in this manner to obtain information as to the condition of the skin vessels, especially in relation to their permeability, in such abnormal conditions. Other methods have been used to determine vascular permeability:[2] 1. The distribution into the tissue of dyes injected into the blood stream. 2. Changes in the blood concentration under varying conditions. 3. The injection of fluids into the tissues and later withdrawing them and determining the changes that had taken place. 4. The determination of the blistering time of the skin.

Because of its simplicity and rapidity of action, the wheal method was used in this investigation in a large number of infants and children, including normal children and those showing a variety of pathologic conditions.

As it is well known, wheals are produced by a large number of unrelated substances, notably histamin, members of the morphin group and proteins, the latter at times being specific. Familiarity with the use of the morphin group in a previous work [1] led to the choosing of codein (whose action is identical with morphin) as the whealing agent. The quantity of the drug injected at any time was too small to produce symptoms or signs of systemic action.

Description of the Codein Reaction.—Shortly after the intradermal injection of 0.15 c. c. of a 1:1,000 codein solution, a flush appears, which

* Received for publication, Oct. 14, 1925.

* From the Babies' and Children's Hospital and the Department of Pediatrics of Western Reserve University and Lakeside Hospital.

1. Pilcher, J. D., and Sollmann, Torald: The Skin Reaction to Morphin, Arch. Int. Med. **33**:516 (April) 1924.

2. Müller, O.: Die Kapillaren der menschlichen Körperoberfläche, Stuttgart, F. Enke, p. 104. The book gives an extensive description of the skin vessels under many pathologic as well as normal conditions.

is soon followed by a wheal at the site of injection; the flush reaches the maximum usually within five minutes, the wheal a little later; in from ten to fifteen minutes, the flush begins to fade, the wheal loses its sharp outline and gradually both disappear, the wheal outlasting the flush. Normally, the wheal has entirely disappeared in an hour or somewhat longer. The wheal averages from 1.1 to 1.3 cm. and the flush from 3 to 5 cm. in diameter, and there may be considerable variation among normal persons. The brief duration of this phenomenon permits the study of a large number of reactions in a reasonable period of time.

The Nature of the Reaction.—During the course of this work, the excellent article on wheal formation by Lewis and Grant [3] appeared, in which they describe the physiologic changes produced in wheal formation and the various physiologic states that could alter the reaction. In urticarial subjects they used simple stroking as a mechanical agent, and the intradermal administration of histamin solutions by needle puncture as a chemical agent. They conclude that these agents produce a characteristic series of independent phenomena, namely, (1) Local dilatation of capillaries, venules and arterioles by direct action; (2) widespread dilatation of neighboring arterioles by local reflex action; (3) increased permeability of vessel walls by direct action.

The similarity of codein and histamin whealing has been noted by Sollmann and Pilcher,[4] using the scratch and mucuna methods. In view of Lewis and Grant's work on histamin, it seemed advisable to compare the wheal production of codein and histamin, using their puncture method and the intracutaneous injection method used in this work under certain conditions they introduced. In a series of five subjects, it was found that solutions of codein, 1:1,000, and of histamin, about 1:4,000, gave very similar reactions as to time of onset, general appearance and fading time of the wheals and the flushes. The reactions were also quite alike in one subject who had given an unusually marked reaction with codein, and in a second subject who had a much lessened codein reaction because of edema.

Adequate circulation is necessary for wheal production, as shown by Lewis and Grant.[3] Impairment of the circulation modifies the wheal production of codein and histamin essentially to the same degree. When the circulation in the forearm is lessened by a pressure of from 70 to 90 mm. of mercury by a cuff applied to the upper arm, no wheal occurs when codein (1:1,000) and histamin (1:3,000) punctures or intradermal injections are made; with lower pressures in the cuff, wheals are slower in forming and are smaller.

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3. Lewis, T., and Grant, R. T.: Heart **11**:209 (May) 1924.

4. Sollmann, Torald, and Pilcher, J. D.: J. Pharm. & Exper. Therap. **9**: 309 (March) 1917.

At the beginning of this work, it had been assumed that the edema of the codein wheal was caused by increased permeability of the walls of the vessels of the skin in the presence of adequate circulation, but no proof for this assumption was at hand. Müller [2] had given the same explanation without giving proof. Lewis and Grant [3] present proof that the essential factor in the wheal edema of histamin as well as that of stroking is the increased permeability of the vessel walls, as opposed to exaggerated filtration pressure. They found that an external pressure of about 50 mm. of mercury was necessary to prevent wheal production; at pressures of 35 mm., definite, though reduced, wheals were formed. The pressure was exerted by applying a sphygmomanometer cuff at once directly over histamin (1:3,000) punctures and holding it there for four minutes (at which time a normal histamin puncture wheal is well developed); on removing the cuff no wheal had formed but did form then. Somewhat lower pressures than this sufficed to prevent wheal production from intradermal codein (1:1,000) injections; in one subject definite wheals formed under a pressure of 30 mm. of mercury, but they were little elevated, while at 20 mm. the elevation was considerable although not equal to that of a wheal forming without pressure. In a second subject, wheal production was very slight until the external pressure was reduced to 15 mm. of mercury.

Microscopic Examination of the Wheal Area.—The microscopic picture of the minute skin vessels in urticarial wheals has been described in the literature.[2] The wheal area from codein was examined for comparison and the findings agreed with those reported. After an intradermal codein injection a short distance from the finger-nail bed, the long vascular loops dilated distinctly and gradually disappeared from view as the wheal edema spread to the nail bed. On the dorsum of the finger at the border of the injection wheal, the vascular tufts increased somewhat in size and more of them became visible and the field assumed a redder tint; gradually the tufts faded as the edema increased and the field became much lighter in color. Toward the periphery, in the flushed area away from the wheal, the tufts were distinct and the field was much redder.

Distribution of the Injected Fluid in the Wheal.—To determine this point, injections of the usual codein solution (1:1,000), containing 1 per cent. or more of methelyn blue, were made into the skin of two subjects in several experiments. The wheal was tinged blue, a deep blue at the injection site and a much paler blue toward the wheal periphery. As the wheal fluid was absorbed, the blue color at the periphery became more intense, probably because it became more concentrated as the fluid was absorbed. This was considered to indicate that the injected solution diffused throughout the wheal area, and that the increased vascular permeability was a direct action of the injected fluid.

Experimental Procedure.—Routinely, codein sulphate was used in a 1 : 1,000 dilution in saline solution containing 0.25 per cent. tricresol. Uniform quantities, usually 0.15 c. c., were injected into the skin (intradermally) of the forearm toward the elbow; this site was chosen merely as a matter of convenience but the same site was always used unless otherwise stated, as the skin in different parts of the body may react differently to local irritants, as it does to tuberculin;[5] the skin toward the wrists, for instance, gives a much less wheal reaction with codein than that near the elbow. Control injections of the tricresol-saline solution were also made. The time of onset, the dimensions of the wheal and flush, and the disappearance time of the same were recorded. More important than the area of the wheal was the degree of fullness or elevation above the surrounding skin, for this gave a much better conception of the amount of exudation than did the area of the wheal; as under certain conditions broad flat wheals were formed in which the total exudate was slight, and again a very well elevated wheal, though of small area, gave evidence of considerable exudate. These facts will be discussed as necessary in the text. A large number of injections of a dilution of 1 :1,000,000 were made to test the susceptibility of subjects to dilute solutions, for it was found in previous work that an occasional subject reacted somewhat more to this dilution than to the control injections. However, it was again found that this added little to the facts learned from the 1 :1,000 solution and it was discontinued as a routine procedure.

EDEMATOUS INFILTRATION OF THE SUBCUTANEOUS TISSUE

In a previous paper [1] it has been shown that codein wheal formation was either lessened or abolished by the presence of edema of the subcutaneous tissue, roughly proportional to the extent of the edema. These observations were limited to subjects with edema of cardiac origin, and it seemed of interest to extend the observations to edema of other types. Experiments were therefore made on subjects with anasarca, that is infiltration of the subcutaneous tissue, as caused by saline infusion, serum uticarial wheals, nephritis, starch feeding injury, leukemia and further observations in cardiac edema. In a separate section, data on subjects with skin infiltration of a different nature, namely, in cretinism and in sclerema, will be presented.

Skin Infiltration from Saline Infusion.—Subcutaneous infusions, of course, do not produce a true edema of the skin but merely an infiltration and probably have no direct effect on the minute vessels. However, in this condition wheal formation was much lessened, just as in true edema of the skin. The experiment was made as follows:

5. Salmony, L.: Arch. f. Kinderh. **69**:454 (June) 1921.

An undernourished infant, white, aged 2 months, had received a saline infusion into one side (left) of the abdominal wall; ninety minutes later, while the tissues were still somewhat boggy, an intradermal codein injection was made over this area and into the normal skin on the opposite half of the abdominal wall. On the infiltrated side a flat wheal, 1.0 cm. in diameter, and a pale flushed area 2.5 by 3 cm. appeared; on the normal side the wheal was 1.3 by 1.4 cm. and the flushed area was 3 by 3 cm.; the latter wheal was much fuller and the flush more intense and remained for a longer time. Two days later, similar experiments were made, the infusion being on the opposite side (right); however, wheal formation was again much less on the infiltrated side. Simple infiltration of subcutaneous tissue, therefore, lessens wheal formation and hastens the disappearance time of the wheals.

Wheal Formation in Serum Urticarial Lesions.—When the skin is edematous and the vessels dilated from serum urticarial wheals, codein has very little effect. This was strikingly illustrated in a boy, 10 years of age, who was suffering from extensive urticarial lesions after injections of meningococcus serum. The subjects skin was not hypersusceptible to codein during this period, that is, the action of the serum did not increase the susceptibility to another type of substance producing wheals. The general appearance of the serum and the codein wheals, and the fact that the serum wheal was but little changed by the additional stimulation of the codein, suggests that the two substances act on the same vascular structures.

While in the acute stage of urticarial lesions, codein injections were made into (1) normal skin, (2) fully formed serum wheals, and (3) fading serum wheals.

1. The normal skin presented the usual wheals and flushed areas that were indistinguishable from the serum wheals; the disappearance time was somewhat more than sixty minutes, that is, about normal. 2. The serum wheal showed a little more fulness than before the codein injection, and this wheal seemed to be a bit more elevated than other serum wheals; no true codein wheal was formed, however; no difference could be observed between the flush in this and in the other serum wheals. 3. The codein injection into the fading serum urticarial wheal gave about the same results as in the fully developed serum wheal. Active infiltration of the skin by serum of urticarial lesion, therefore, lessens the wheal reaction of codein.

Edema of Nephritic Origin.—Wheal formation was also lessened in this type of edema in several subjects. One subject with acute diffuse nephritis was examined a number of times and at various stages of the edema as it progressed from what was considered to be very mild or

occult edema (the feet pitted on pressure but the forearms did not), to the severe stage when the forearm was much swollen and pitted readily on pressure. In this patient during the occult period of edema, the wheals were of average size but were rather flat and disappeared in about one-half the normal time. When the skin edema was marked, wheal formation and flushing were very slight or absent and the disappearance time was much shortened. Similar results were obtained in experiments on other nephritic patients.

Edema from Starch Injury (Czerny's Mehlnährschäden).—The following case of decomposition from starch feeding injury is reported, although there was no demonstrable edema present, except probably in the cheeks, but the condition is often associated with manifest edema. On admission, the wheal reaction was very slight but gradually increased with improvement in the infant's condition until an unusually marked response to codein was present. The subject was an infant, aged 12 months, weighing 5,000 gm., who was seriously ill from the hypertonic type of starch injury; the skin was loose and dry with little subcutaneous tissue but a peculiar doughy feel, although there was no pitting on firm pressure. The puffiness of the cheeks usually seen in this condition was present.

Three codein injections made within a week gave slight reactions, the wheal measuring 1 by 1.1 cm., showing fair dispersion of the injected fluid, but they were flat and did not become indurated; the flushing (reflex vascular dilation) was practically absent; the disappearance time was quite short, less than thirty minutes. Three weeks later, when the general condition had greatly improved and the patient had gained 1,300 gm., the reaction was very marked, for the wheal was elevated much more than in the average infant and the disappearance time had increased to sixty minutes; the flushed area was about normal and was a bright red, in strong contrast to the previous practical absence of flushing. This reaction, as regards the elevation of the wheal, was as marked as had been seen. At this time also, the reaction to a 1:1,000,000 dilution which had previously been negative, became positive. In another week, with a further gain of 960 gm., the whealing was still great, the disappearance time prolonged to more than sixty minutes and the area of flushing more marked also. Throughout the illness, the diameter of the wheal was about the same, indicating that at all times the injected fluid was well dispersed. It is concluded that the lessened wheal formation in the acute stage of the illness was due to the increased water content of the skin.

Edema in Leukemia.—Wheal formation was also lessened in one subject with acute lymphatic leukemia, who had slight edema of the forearms as well as of other parts of the body. In other leukemic patients,

without edema, wheal formation was not lessened, so that this exceptional result was attributed to edema and not to any factor inherent in the leukemia itself.

Edema of Cardiac Origin.—As stated previously, edema of cardiac origin lessens or abolishes codein wheal formation roughly proportional to the degree of edema. This observation was confirmed in the present work, but need not be further discussed.

It is thus seen that edema of the skin, regardless of the nature or origin so far as has been studied, decreases the wheal reaction of codein. Several factors would seem to be involved in the phenomenon. With edema, the minute skin vessels may be compressed sufficiently to lessen the circulation and hence diminish wheal formation. In such circumstances, too, it is conceivable that the tissues and interstitial spaces are already distended with fluid and do not readily take up more. It is not a question of failure of the injected fluid to disperse, for in the milder stages of edema wheals may be of the same surface extent as in normal subjects, and in severe grades the injected fluid is very well dispersed and at times no injection wheal can be formed. Dilution of the codein solution by the edema fluid would, of course, lessen the extent of wheal formation. In cases of slight or nondemonstrable edema there may be other factors not disclosed at present. It is hardly conceivable that at certain stages of the edema the vessels are less permeable, for the phenomenon of decreased wheal formation is a constant one, that is, it is present at all stages. The local swelling of the skin by urticaria interferes with wheal productions by codein in the same manner as do other edemas.

McClure and Aldrich [6] have reported that intracutaneous injections of saline solution disappeared more rapidly in the presence of edema than in the normal skin. The edema occurred in cardiac and in renal disease and in anemia. In a later communication,[7] these investigators have pointed out that "When tests were made on patients with developing edema, a reduction of the disappearance time preceded other clinical evidence of edema by several days. In improving edematous cases, increased disappearance time had been observed before the edema showed any apparent decrease." Their studies were in patients with nephritis. These two studies are in agreement as regards disappearance time of wheals whether from injected saline solution merely or from those formed by an active exudate from codein irritation. Following their publications, other papers have appeared on the disappearance time of

6. McClure, W. B., and Aldrich, C. A.: Time Required for Disappearance of Intradermally Injected Salt Solution, J. A. M. A. **81**:293 (July 28) 1925.

7. Aldrich, C. A., and McClure, W. B.: The Intradermal Salt Solution Test, J. A. M. A. **82**:1425 (May 3) 1924.

intradermal saline solutions under various conditions such as scarlet fever and diphtheria,[8] pneumonia [9] and, as this article was written, for determining the circulation in the extremities.[10]. The interpretation of results in similar conditions is given in another section.

INFILTRATION OF THE SKIN

A number of subjects had infiltration of the skin differing from the skin edemas described in the previous section. The infiltration was of two types, that of cretinism and myxedema, the characteristics of which are readily understood without further description, and a second type of a much firmer infiltration or induration resembling sclerema.

Cretinism.—In a previous work, an adult with myxedema, without any great change in the skin that was discoverable to touch or sight, gave a somewhat lessened reaction to codein. This brought the query as to whether patients suffering from lack of thyroid secretion present abnormalities of the skin that would lessen the codein wheal reaction; it was considered at the time that the so-called edema of the skin could be the causative factor in lessening wheal formation. In the present study, several cretins of different degrees of severity were examined, and the conclusion is drawn that in all probability it is the edema or infiltration of the skin, the nature of which seems not to have been fully determined, that lessens the wheal phenomena.

In the most striking case the results were as follows: An infant, aged 6 months, a cretin, had dry, thick, nonpitting skin, a short neck, a thick, partially protruding tongue and was physically and mentally inactive. Five injections of codein 1 : 1,000 on different days gave very slight reactions; the wheals were small in area, flat, nonindurated; the erythema about the wheals was just discernible and not more than 1.2 cm. in diameter; both wheals and flush disappeared within twenty minutes in all cases; two injections of codein 1 : 100, which causes a very marked reaction in normal subjects, gave no greater reactions. Unfortunately, the patient died from an intercurrent infection before the results of thyroid medications became evident, either clinically or to the codein reaction. Three other cretins of less severe grade were examined, children aged from 7 to 12 years; all had basal metabolism from 11 to 20 per cent. below normal. One of them in whom the skin, though fine and rather delicate, seemed to have more than the normal amount of subcutaneous tissue gave a lessened reaction. The skin of

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8. Baker, W. J.: Intradermal Salt Solution Test in Scarlet Fever and Diphtheria Patients, J. A. M. A. **83**:1566 (Nov. 15) 1924.

9. Harrison, J.: Intradermal Salt Solution Test in Lobar Pneumonia in Children, J. A. M. A. **84**:1258 (April 25) 1925.

10. Cohen, M. B.: The Intracutaneous Salt Solution Test, J. A. M. A. **84**: 1561 (May 23) 1925.

the other two was scarcely suggestive of the myxedematous state and the wheal formation was about normal, although the flushing about the wheal, while of average extent, was pale and disappeared somewhat more rapidly than usual.

It is concluded, therefore, that the codein wheal reaction is diminished in cretinism and myxedema when the characteristic skin infiltration is present. The mechanism of this diminution is considered to be similar to that of simple edema, and probably does not depend on a decreased permeability of the vessels or on any factor peculiar to lack of thyroid secretion. Von Gröer and Hecht [11] report no decreased sensitivity to morphin in myxedematous children; the children must have had normal skins, free from the peculiar edema of the untreated myxedema state.

Scleredema and Sclerema.—Under this heading are classed four patients, on one of whom only was a definite diagnosis of scleredema made, but the state of the skins of the others strongly suggested a mild degree of sclerema. In each patient the vascular reaction was greatly lessened over the affected region, but was normal or approximately so over the normal parts in three subjects who had areas of normal skin. The minimum whealing in these patients was probably due to the firm structure of the skin and subcutaneous tissue which prevented collection of serum in the intercellular spaces or in the cells themselves, with the possibility of insufficient circulation playing a rôle, although there was no definite evidence of insufficient circulation in the parts examined. The principal features of these cases are as follows:

Scleredema.—An infant, negro, aged 2½ months, weighing 7 kg., was born with swollen feet. Both feet and lower part of the legs were greatly swollen, with tense and shiny skin, and pitted only with much pressure. The infant otherwise was normal. Much pressure was needed to make the injection; the injection sites blanched over an area 1.1 by 1.2 cm., but no wheal was raised and the skin returned to normal in about ten minutes. Similar injections in the forearm where the skin was normal gave reactions somewhat above the average.

Sclerema.—One subject was an undernourished negro infant, the skin of whose entire body seemed somewhat firmer than normal and was indurated; that of the legs was much more so, especially the right which was decidedly hard and indurated. Much pressure had to be used in making the injection and the injection wheal was very little elevated. Wheal formation in the skin of the arms and left leg was somewhat below normal, while that of the more indurated right calf was decidedly abnormal consisting merely of a pale area 0.7 by 0.9 cm., that is, below

11. Von Gröer, F., and Hecht, A. F.: Ztschr. f. d. ges. exper. Med. **33**:1, 1923.

normal size, without elevation or induration; the flush in this leg was also less than on the opposite leg.

An infant, white, aged 10 weeks, much undernourished, was in a state of decomposition, and weighed 3,900 gm., that is, practically the birth weight; the skin was dry, thick, firm and in folds, with very little subcutaneous tissue, the condition corresponding well with a mild degree of sclerema. Two series of tests were made at ten day intervals, and in each test much pressure was required to force the fluid into the skin. In each case the wheals were quite small, scarcely becoming elevated; the flushing also was slight, the disappearance time much less than the normal.

An infant, negro, aged 9 months, was moderately ill from acute bronchitis. The skin of the legs was tense and shiny but did not pit; this condition did not suggest a simple edema and no cause for such was present. On three separate days (4 experiments in all) wheals similar to those of the first patient of this series were found; there were pale areas about the injection site, 1.2 by 1.5 cm. in diameter, but with slight or no elevation of the wheal site; at the same time wheal formation in the skin of the forearm, which apparently was normal, was above the average extent (1.2 by 1.5 up to 1.3 by 1.9 cm.) and the wheals were well raised.

It seems, then, that dense infiltration of the skin or subcutaneous tissue as well as simple edema or myxedematous infiltration definitely diminishes the wheal reaction.

NEPHRITIS

One of the causes of edema in nephritis has been stated to be increased vascular permeability. In nephritis of the glomerular type, as well as in other diseases, Morawitz and Deneke [12] found a change in the concentration of the blood following a compression of the vessels of the upper extremity, indicating to them an increased vascular permeability. Müller [2] states that in many abnormal renal conditions the minute skin vessels are damaged as well as those of the kidney; he also attributes the edema of nephritis to the increased permeability of the minute vessels. Several cases of nephritis of different types without clinical evidence of edema have been studied in this work, but no departure from the normal vascular permeability could be determined by the codein wheal method. The series is not large, as all cases with suggestion of edema were excluded. These subjects include five cases of acute glomerular nephritis, two acute and one severe chronic diffuse nephritis and one uremia. The experimental results are as follows:

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12. Morawitz and Deneke, quoted from Loeb, L.: Monograph on Edema, Medicine **2**:171 (Aug.) 1923.

Glomerular Type.—Two boys, negro, each aged 3 years, were subjects of acute glomerular nephritis; the urine of each contained much blood and albumin and but few casts; there was no clinical evidence of edema. The wheal formation in each case was of the spreading variety, that is, they were of large diameter (1 by 1.8 and 1.2 by 1.9 cm.), but neither was well elevated nor indurated; the disappearance time was a little under one hour in one boy and a little over one hour in the other. The reactions were not greater than often found in normal children. One child reacted normally to dilute solutions of codein (1 : 100,000 and 1 : 1,000,000). There was then no evidence of increased vascular permeability nor of edema; neither child developed edema during the course of the illness. The results were similar in a third negro boy with similar urinary findings and with nitrogen retention (81 mg. nonprotein nitrogen per hundred cubic centimeters of blood).

Wheal formation was normal in a young white girl, with less severe glomerular nephritis. The patient had had puffy eyelids and questionable edema of the legs a few days previously, but no demonstrable edema at the time of the experiment. Some ten days later the patient made a rather rapid gain in weight but with a normal urine output, and the question of oncoming edema was considered; however, the wheal reaction was a little more marked than previously and no edema developed. The reaction was also normal in a girl, white, aged 4 years, with a mild glomerular nephritis.

Acute Diffuse Nephritis.—In two subjects with this condition, the wheal formation was modified apparently by invisible edema, for in each subject there was slight pitting of the ankles but none of the forearm. The wheals were of average size but were rather flat and disappeared in about thirty minutes. About two months later, the reaction again was somewhat diminished in one of these subjects, when the forearm was apparently free from edema, but the ankles were still slightly edematous. The child died later, never having become free from edema, and the anatomic diagnosis was diffuse nephritis. The second patient, a girl, white, aged 11 years, was examined sixteen months later when free from edema and the wheal formation was considerably above the average although within the limits found in normal children. At this time the urine contained much albumin, hyaline and granular casts, and white blood cells; the blood creatinin was 1.2 mg. and the nonprotein nitrogen 51.0 mg. per hundred cubic centimeters; the blood pressure was 128 systolic; 85 diastolic.

Severe Chronic Diffuse Nephritis.—The wheal reaction was normal in such a condition in a boy, aged 10 years, who had high blood pressure, albuminuric retinitis and the usual urinary findings. No edema was demonstrable, although the patient was edematous some time previously.

Uremia.—In a single instance of this condition the wheal reaction was normal. An infant, white, aged 14 months, developed acute urinary suppression following osteomyelitis; it was known that no urine had been voided in three days; the blood urea was 280 mg. and creatinin was 3.5 mg.; the subcutaneous tissue was normal, showing no edema nor water loss. The patient died a few hours later without developing edema.

In the different types of nephritis reported, there was no indication of an increased permeability of the vessels of the skin as judged by the codein wheal formation method and it is suggested, therefore, that increased vascular permeability is not the cause of edema in nephritis.

CARDIAC DISEASE

Valvular cardiac disease, even with rather marked decompensation, does not of itself influence wheal formation; with severe myocardial involvement, however, wheal formation is diminished as a result of the lessened circulation. These conclusions were drawn from a study of a group of seven subjects with chronic valvular disease, all of whom showed definite decompensation and but one of them evidence of more than slight myocardial degeneration. Several infants with compensated congenital heart disease were also examined. All subjects of this group, of course, were free from edema.

Valvular Lesions Without Myocardial Degeneration.—This group of six children gave wheal reactions within the normal limits; in fact in three instances the reactions were rather above than below the average; the wheals were of good size and elevation and the flush was wide, although often pale as a result of the subject's anemia. Two subjects were somewhat more susceptible to minimal codein solutions than the average person. The valvular lesions included aortic and mitral insufficiencies and mitral stenosis, as is stated in Table 1, in which the details are presented; no patient with aortic stenosis was examined. As is evident from the previous statements, the nature of the valvular lesion or lesions and the valve involved did not influence the results. The degree of decompensation was sufficient to require rest in bed in the hospital at the time of the examination; orthopnea was present in all cases, but severe in one case only. The patients were discharged later to their homes or to a convalescent hospital.

Valvular Lesions with Severe Myocardial Degeneration.—In the only patient with this condition, the wheal reaction was definitely diminished; the wheals were neither elevated nor indurated, the flush was slight and the disappearance time was much shortened. The subject was a boy with mitral and aortic insufficiencies, myocarditis and pericarditis. The forearms were very slender, and they and the legs and feet were

definitely without evidence of edema. Against advice, the patient was taken from the hospital, and died a few weeks later.

Congenital Heart Disease.—Two infants with this condition reacted possibly somewhat above the average. One of them was moderately well nourished; there was deep cyanosis of the extremities, lips, mucous membranes of the mouth and tongue, and there were innumerable petechial hemorrhages over the entire body; the extremities were moderately warm; the pulse was just palpable at the wrist, and the systolic blood pressure was not more than 50 mm. of mercury, although the infant was in excellent condition. The second infant was somewhat undernourished, but aside from loud cardiac murmurs gave no evidence of circulatory involvement. Two other infants with congenital heart disease gave average reactions. It is evident then that congenital heart disease does not of itself influence the codein wheal reaction.

TABLE 1.—*Data of the Wheal Reaction in the Cardiac Group*

Subject	Age in Years	Lesion	Wheal		Flush	Disappearance Time in Minutes
			Diameters in Cm.	Induration*	Diameters in Cm.	
2	7	Mitral stenosis and insufficiency	1.4 × 1.7	+ +	4 × 5	60+
45	11	Mitral and aortic insufficiency	1.1 × 1.7	+ +	3.5 × 8	60
26	11	Mitral and aortic insufficiency	1.0 × 1.1	+ +	3 × 5	60
87	13	Mitral insufficiency	0.9 × 1.4	+ +	3 × 4	60
79	13	Mitral stenosis and insufficiency	1.4 × 2.4	+ +	5 × 8	60+
15	8	Myocarditis, aortic and mitral insufficiency, pericarditis	1.0 × 1.1	+	2 × 3	40
			1.0 × 1.3	+	3 × 4.5	40
70	6 mo.	Congenital heart; no cyanosis	1.0 × 1.2	+ +	2.5 × 2.5	60
106	3 mo.	Congenital heart; cyanosis	1.2 × 1.7†	+ +	2.5 × 2.5	60+
			0.9 × 1.6	+ +	2.5 × 2.8	60+

* The size of the wheal is difficult to express as the wheal area gives but two dimensions, the elevation and induration not being indicated by the area: for this reason, in the table + + indicates average and + slight elevation and induration.

† The wheals were diamond shaped, and hence give a somewhat exaggerated idea of the size.

Explanation of the Results in Cardiac Subjects.—From the results, it is concluded that normal wheal formation in this group of subjects was evidence of an efficient circulation, and diminished wheal formation evidence of an inefficient circulation, for, as was pointed out in the introduction, an efficient circulation in the skin is necessary for wheal formation. This explanation is supported by the work of Stewart,[13] who found that the flow of blood in the hand in heart disease was "deficient in cases in which there is evidence of serious impairment of the myocardium, or more comprehensively and probably more accurately of the mechanism on which the force and rhythm of the heart's action depends, even when valvular lesions are absent, than in cases in which gross valvular lesions exist while the heart's action is strong and orderly. This holds even when in valvular disease clinical symptoms of loss of

13. Stewart, G. N.: Studies on the Circulation in Man, Arch. Int. Med. **13**:1 (Jan.) 1914.

compensation are present." In six of the subjects here reported the wheal reaction was normal; these were all subjects with valvular disease with no evidence of severe myocardial involvement or prostration, although the valvular lesions were extensive and there was definite decompensation. The latter would seem to indicate that the circulation in the skin at the site of the wheal reaction at least, remains normal, although the general circulation is not adequate for bodily activity. The normal wheal formation in the subjects with congenital heart disease also indicates an efficient circulation in the part (forearm) examined. The relation of blood pressure to wheal formation is discussed in the following section.

SUBJECTS WITH SEVERE PROSTRATION

The wheal reaction in certain states of severe prostration is very well illustrated in a group of patients who were all very ill either from acute or from chronic illness. The group includes chronic tuberculous peritonitis, miliary tuberculosis, peritonitis with pyelitis, acute lymphatic leukemia, acrodynia, pneumonia, meningitis, one very severe upper respiratory infection and cases of decomposition. The majority of these patients died without improvement, so that control experiments on the same patients in better condition could be made in only three instances. However, other patients with the same diseases but in better condition served as controls in several instances, notably, those with acrodynia, leukemia, pneumonia and pulmonary tuberculosis. In all of these subjects the wheal reaction was much lessened, both the wheal formation and flushing, with a lessened disappearance time also. In all cases the amount of the exudate was much lessened, the wheals being quite flat and not elevated; in part of the experiments the wheal area was small, in others large, showing in the latter that the injected fluid was well diffused but that it did not provoke the usual exudate. The flushing was lessened in extent and in degree, that is, instead of the usual bright red flush it was a pale red and at times very faint. The data are given in Table 2. Before discussing this group, it will be well to describe several of the patients.

REPORT OF CASES

CASE 1.—The patient, a mulatto, aged 8 years, was in the hospital for several months with tuberculous peritonitis; she was very emaciated, the forearm was almost without subcutaneous and muscle tissue, and midway between elbow and wrist measured 10.5 cm. in circumference, less than that of a normal infant aged 6 months. The wheals were all very flat and without induration but varied in size, as it was impossible to make strictly intracutaneous injections each time; the disappearance time was less than thirty minutes. Although the skin was of a light mulatto shade, not black, no flush could be discerned about any wheal.

CASE 2.—Another patient, a girl, aged 5 years, had been ill for some weeks with pyelitis and ulcers of the cecum, with subsequent general peritonitis; she

was much undernourished; the red cells were three million, hemoglobin 55 per cent.; blood pressure, 82 systolic, 50 diastolic; temperature 38.6 C. The wheal was full sized but flat and not indurated; the flush was fair sized but very pale.

CASE 3.—A boy, white, aged 2 years, had acute lymphatic leukemia; the white cells were 59,000, with 95 per cent. lymphocytes; three million red cells, hemoglobin 40 per cent. The boy was fairly well nourished, and had no edema; there were petechial hemorrhages around the mouth and on the legs. The wheal was of average size but flat; the flush was of fair size but pale; disappearance time was lessened.

CASE 4.—A girl, white, aged 2 years, had very severe acrodynia of nine months' duration. The patient was much depressed and somewhat undernourished; the skin of the hands was cyanotic, and was cold and wrinkled like that of a washerwoman; the skin of the forearm was cold and clammy and

TABLE 2.—*Data on Wheal Formation in Circulating Depression Series*

Patient	Age in Years	Diagnosis	Wheal: Diameter in Cm.	Wheal: Induration*	Flush, Diameter in Cm.	Disappearance Time in Minutes	Remarks
46	8	Peritonitis (tuberculous)	0.9 × 1.0	+	.....	15-30	Death a few weeks later
100	5	Pyelitis, peritonitis	1.1 × 1.6	+	3 × 4 faint	40	Death four days later
57	2	Acute lymphatic leukemia	1.0 × 1.5	+	3.5 × 4 faint	50	Death next day
79	2¼	Acrodynia.....	0.9 × 1.2	+	Very faint	60	Death in few hours
93	2	Very severe upper respiratory infection	1.1 × 1.7	+	3 × 4	60	Second experiment made after patient had recovered from illness
			1.1 × 1.7	+++	4.5 × 5 bright red	100	
104	5	Pneumonia.....	1.2 × 1.2	+	2 × 2	30	Recovery. Second and third experiments made after recovery
			1.0 × 1.2	+	2.8 × 3.0 faint	40	
		Anemia.....	1.0 × 1.3	+ +	3.8 × 4	60	
			1.2 × 1.4	+ +	3.2 × 3.8	60	
			1.0 × 1.3	+ +	3 × 4	60	
			1.1 × 1.3	+ +	3.5 × 4 redder	60	
54	13 mo.	Bronchopneumonia	0.8 × 0.8	+	.....	20	Death
103	14 mo.	Meningitis.....	0.9 × 1.1	+	2 × 3.7	45	Death second day after
			0.9 × 1.1	+	3 × 3.5 pink		
113	..	Decomposition.....	0.8 × 0.8	+	.....	30	
			0.9 × 1.2	+ +	.....	60	Four days later
			0.9 × 1.3	+ +	.....	60	Seven days later

* The size of the wheal is difficult to express as the wheal area gives but two dimensions, the elevation and induration not being indicated by the area: for this reason, in the table + + indicates average and + slight elevation and induration.

was of tough consistency; the temperature was normal. The wheal was of average extent, rather flat, but more striking than the lessened wheal formation was the slight flush that was just a narrow border of faint red about the wheal; the flush disappeared in less than fifteen minutes but the wheal persisted for sixty minutes. Several needle punctures with a solution of codein 1:100 gave rather flat wheals of a maximum of 2.0 mm. in diameter, with very little flush. The disappearance time was thirty-five minutes. In a control patient the wheals from similar codein punctures were 3.0 mm. in diameter with a flush of 2 by 2.5 cm., and a disappearance time of seventy-five minutes.

CASE 5.—A girl, aged 2 years, well nourished, was very severely ill with an upper respiratory infection; the hands and feet were moist, cold and cyanotic, although external heat applied just before the experiment had improved their condition somewhat; the pulse was feeble; the temperature was 40 C. (104 F.).

The wheal was of good size but was not elevated nor indurated; the flush was smaller and less vivid than normally; disappearance time was sixty minutes. The child made an excellent recovery, and in eighteen days had gained 400 gm. in weight; the skin was fine and warm and the child was well nourished; the pulse and temperature were normal. At this time, wheals were of the same diameter as previously, but were well raised with considerable induration; the flush was larger and a bright red; the disappearance time increased from sixty minutes to more than 100 minutes, that is, longer than in the average subject.

CASE 6.—A boy, white, aged 5 years, was very ill with pneumonia and secondary anemia from intestinal hemorrhages; the red cells were 2,800,000; hemoglobin not more than 50 per cent.; blood pressure was 90 systolic, 48 diastolic; the wheals at this stage were decidedly flat and the flush was just discernible. With recovery that was very gradual, the hemoglobin increased to 65 per cent., blood pressure to 112 systolic, 60 diastolic, and the general condition was much improved; the wheals became more indurated and the flush wider and of a deeper red.

CASE 7.—An infant, negro, with decomposition, was markedly dehydrated when first examined and the wheal reaction was very slight. The infant's condition improved rapidly, and within four days the wheal reaction was somewhat above the average and remained so.

Similar striking results were seen in a very dehydrated premature infant who improved rapidly in the hospital. The study of the wheal reaction in dehydrated subjects is being continued.

Explanation of the Lessened Wheal Reaction in this Group.—Among the physiologic conditions that diminish wheal formation, lessened blood flow is of the greatest importance, and this is considered to be the essential cause of the diminished wheal formation in this series of cases. The actual blood flow in the arm examined was not determined, but the conclusion, that the flow was lessened, is drawn because the patients were very feeble from chronic illness or were severely prostrated from acute illness. In individual cases, certain factors give definite indication of the diminished blood flow. The patients with acrodynia and the severe upper respiratory infection had cold, clammy, cyanotic extremities, and Lewis and Grant [3] have shown that cooling of the skin lessens wheal production, which they attribute to the same factor, namely, lessened blood flow. Ebbecke [14] has pointed out the relationship between the color and temperature of the human skin and the state of the vessels; in the cold, blue hand such as in the two patients under discussion here, he found the arterioles to be strongly contracted, with the capillaries and venules dilated, and a much decreased circulation.

Stewart [15] describes a subject with a great decrease in blood flow to the hands; a woman, aged 72, "who showed the typical skinny hand of old age, with feeble pulse." This description corresponds well to the skinny hand and forearm of the colored child with tuberculous peritonitis, whose pulse was feeble also; however, the analogy is not complete, for the elder subject had cardiac arrhythmia and arteriosclerosis.

14. Ebbecke: Arch. f. d. ges. Physiol. **169**:1, 1917.

15. Stewart, G. N.: Heart **3**:33, 1911.

It seems reasonable, however, to attribute the decreased wheal formation in this subject to decreased blood flow. The wheal formation in the subjects with decomposition is also probably due to decreased circulation, for Utheim [16] has shown that the circulation in such conditions is decidedly decreased. The essential factor in the decreased blood flow in these instances (decomposition) was considered to be lack of blood volume, for the patients were severely dehydrated; in other subjects with decomposition who were not severely dehydrated, no such lessened wheal reaction showed.

Anemia lessens the blood flow in the hands (Stewart [17]), and this feature may have been an additional contributing factor in three subjects whose red cells were only from 2 to 3 millions and hemoglobin from 40 to 55 per cent. Anemia of this degree has not materially altered the wheal reaction in other subjects, however, so that it probably was not the primary cause of the lessened wheal reaction in these patients. There has not been sufficient opportunity to date to study severe uncomplicated anemias. The low hemoglobin probably explains the unusual paleness of the flushed area noted in this group and in other anemia subjects.

The effect of fever has been considered as a factor in lessening the wheal formation, as several of these patients had temperatures above normal, up to 40 C. (104 F.) in one instance, and Stewart,[18] has demonstrated that fever usually somewhat decreased the blood flow in the feet. While the study of the effect of fever has not been completed, whealing was not greatly modified in other fever subjects, so that fever was not considered to have been the direct cause of the lessened wheal formation in the subjects under discussion. However, it is not improbable that the constriction of the skin vessels during certain fevers might decrease the blood supply sufficiently to lessen the size of wheals, and when the skin is hot and flushed the opposite may be true. The latter was thought to be the case in an infant, colored, severely ill with pulmonary and general miliary tuberculosis, who had shown the flat, nonindurated wheals which have been interpreted as due to lessened circulation; such wheals were formed on five separate days, each time with temperature of from 38 to 39 C., but the forearms were not noted to be abnormally warm or cold; shortly before death, when the forearm was distinctly hot and the temperature was 39 C., a well elevated indurated wheal was formed.

The question of the relation of blood pressure and wheal formation has not been decided in patients, except as has been pointed out in the

16. Utheim, K. A.: A Study of the Blood and Its Circulation in Normal Infants and Infants Suffering from Chronic Nutritional Disturbances, Am. J. Dis. Child. **20**:366 (Nov.) 1920.
17. Stewart, G. N.: J. Exper. Med. **18**:113, 1913.
18. Stewart, G. N.: J. Exper. Med. **18**:354, 1913.

introduction, that pressures of from 70 to 90 mm. of mercury applied by a cuff to the upper arm abolish codein wheal formation. At best, blood pressure is but one factor in blood flow. The pressure in two members of this group at the time of lessened wheal formation was rather low, 82 systolic, 50 diastolic, and 90 systolic, 58 diastolic, but was not recorded in the other subjects. Other persons, however, have shown fair wheal reactions with similar low pressures, notably in one subject with congenital heart disease who presented an excellent wheal reaction when the systolic blood pressure could be determined at no more than 50 mm. and the radial pulse was just palpable. The relation of blood pressure to wheal formation must be deferred for further observations.

The Wheal Formation in Subjects with a Positive Reaction to Tuberculin.—Susceptibility to the intracutaneous tuberculin reaction apparently bore no relation to the wheal formation of codein, that is, the wheal formation in the tuberculin positive subjects was neither greater nor less than in the tuberculin negative subjects. This was determined from a study of ten children (from 1 to 13 years of age), who gave a strongly positive tuberculin reaction, and of twenty-five children (aged from 6 months to 13 years) with negative reactions who served as controls. The tuberculin reactions were all strongly positive from the 1:1,000 dilution of tuberculin (old tuberculin) in patients who were subjects of glandular, bone, pleural or pulmonary tuberculosis, and in two subjects with scrofula. The controls were all negative to a 1:1,000 dilution; seventeen of them to a 1:100 and two to a 1:10 dilution. With two exceptions (both of whom had excellent wheals) all patients were fairly well nourished, and no other condition was present which, so far as is known, could have modified the wheal reaction.

Wheal production under a number of other pathologic conditions has been investigated, but the number of subjects in any one condition has not been sufficient to warrant conclusions. The investigation is being continued.

CONCLUSIONS

Wheal formation in the skin is a manifestation of increased permeability and dilation of the minute vessels. An efficient circulation is necessary for wheal formation. A study of wheal formation by the intradermal injection of codein solution was made in a series of normal and sick infants and children. The following observations are reported and conclusions drawn.

1. Wheal formation was lessened in all cases of edema studied, regardless of the cause, namely, in nephritis, cardiac decompensation, leukemia, malnutrition from starch feeding injury and in the local skin edema of serum urticarial wheals and saline infusions. This result is due to the edema of the skin itself and not to decreased vessel permeability.

2. Wheal formation is also lessened in certain ill-defined skin infiltrations, namely, in cretinism and myxedema and in sclerema and scleredema.

3. In nephritis without edema, the wheal formation, and hence the vessel permeability, is normal, indicating that the cause of edema in nephritis is not increased vascular permeability.

4. In valvular and congenital heart disease without edema, even with considerable decompensation, the wheal formation is normal, indicating an efficient circulation in the skin.

5. In myocardial degeneration and in certain cases of severe prostration, wheal formation is diminished because of a lessened circulation in the skin.

6. A normal wheal reaction indicates an efficient circulation at the site of the wheal.

7. The presence of a strongly positive tuberculin reaction does not modify wheal formation.

WHEAL FORMATION IN INFANTS AND IN CHILDREN

II. IN RICKETS AND SPASMOPHILIA WITH LOW SERUM CALCIUM AND PHOSPHORUS *

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CLEVELAND

The effect of calcium on vessel permeability has been the subject of much investigation, the results of which, however, have not always been in accord. The question has recently been thoroughly reviewed in Loeb's [1] excellent monograph on "Edema," and need not be detailed here. It is rather generally accepted that calcium usually lessens the severity of inflammatory skin reactions by irritants such as croton oil, and that it lessens the permeability of cell membranes, although Fleisher, Hoyt and Loeb [1] state that calcium does not influence in a noticeable degree the elimination of fluid from the blood vessels. A more recent research by Tainter and Hanzlik [2] has shown that large subcutaneous or intravenous doses of calcium chlorid had no effect on the development of edema of the face and neck in rabbits from paraphenylenediamin. It has been maintained, notably by Hamburger,[3] that other constituents being constant it is the ionized calcium, not the total calcium, that is concerned in cell permeability. Guenther and Heubner [4] were unable to confirm this observation, and state that the nonionized calcium molecules also have the specific action on cell permeability. As the total serum calcium only was determined in this work, nothing can be added to the solution of this particular phase of the question.

The effect of decreased calcium content in the blood on vascular permeability seems not to have been studied. As the calcium content of the serum of babies and young children is being determined by others [5] in the department of pediatrics, it seemed worth while to study the wheal reaction in those subjects whose serum calcium was below normal, from about one-half to the normal values; some of them on several occasions as the calcium content rose from a low level to normal.

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* Received for publication, Oct. 14, 1925.

* From the Babies' and Children's Hospital and the Department of Pediatrics of Western Reserve University and Lakeside Hospital.

1. Loeb, L.: Medicine **2**:171 (Aug.) 1923.

2. Tainter, M. L., and Hanzlik, P. J.: J. Pharm. & Exper. Therap. **24**:179 (Oct.) 1924.

3. Hamburger, H. J.: Bull. Johns Hopkins Hosp. **34**:226 (July) 1923.

4. Guenther, F., and Heubner, W.: Klin. Wchnschr. **3**:789 (April 29) 1924.

5. Smith, Donalda N.: Unpublished data.

The codein wheal reaction was used as the method of measuring the vascular permeability; the method is described in a former paper [6] and in brief is as follows: An intradermal injection of 0.15 c.c. of a codein solution (1 : 1,000) produces a wheal which reaches the maximum size within five to ten minutes and disappears in about an hour. The wheal is due to increased permeability of the minute skin vessels.

A total of nineteen subjects with low serum calcium were examined, the majority of which (fifteen) were negroes. Controls of two types were used: (*a*) in a series of six subjects who were examined as the serum calcium rose from the low level to the normal or approximately normal level, thus serving in the most satisfactory way as their own controls; (*b*) the results in the entire low calcium group as compared with those in a group of known normal serum calcium (six subjects).

As regards the general condition of these patients, six were somewhat undernourished but none were in a state of decomposition; the remainder were either in an average state of nutrition or were somewhat above the average. All gave clinical and roentgen-ray evidence of rickets and some of them were subjects of spasmophilia.

Group A.—The serum calcium of the six subjects had a minimum value of from 4.9 to 7.1 mg. per hundred cubic centimeters of serum, and after treatment attained a maximum value of from 9.6 to 10.4 mg. at the time of the final experiment. The body weights varied from 6.7 to 13.50 kg. Three of the subjects were somewhat but not greatly undernourished and the others were well nourished. At the final experiment there had been a gain in weight from 0 (one case) to 850 gm. (a maximum of 12 per cent.); this is of moment in the undernourished only, all of whom gained, for an undernourished person with considerable loss of subcutaneous tissue often displays a less marked reaction than a well nourished one; however, there was not sufficient change in the condition of any subject materially to affect the reaction.

The results gave no evidence that the low serum calcium content in any way influenced the permeability of the skin vessels as measured by the codein wheal reaction. It happened that in four of the six subjects the reaction was usually slightly larger when the serum calcium was at a higher level but the difference was not sufficiently marked to be of moment. Furthermore, four of this group gave no reaction to minimal codein dilutions (1 : 1,000,000); it was not tested in others. Nor was the reflex vasodilation, as measured by the extent of the flush about the wheal, modified by low serum calcium. This was learned from the reaction in three white children (one in this group and two in Group B) whose minimum serum calcium content was from 5.4 to 6.8 mg. per

6. Pilcher, J. D.: Wheal Formation in Infants and in Children. This issue, p. 77.

hundred cubic centimeters. The other subjects were negroes, in whom it is usually impossible to distinguish reddening of the skin unless this is marked or the skin is of a light shade; at any rate, no abnormal reddening was observed in the negro series. Citation of the results in two subjects, together with controls, suffice to illustrate the essential features; the facts are presented in the table.

Group B.—About twenty-five experiments were made on ten subjects whose serum calcium was somewhat below normal, but in none of whom it had reached quite the normal quantity at the final experiment. The calcium varied from 5.4 to 8.9 mg. per hundred cubic centimeters,

Data on the Wheal Dimensions and the Serum Calcium Content in Two Subjects with Low and, Later, with Normal Calcium Percentages, and on Seven Subjects with Normal or Approximately Normal Calcium Content

Experiment	Subject's Age in Months	Date of Experiment	Subject's Weight in Gm.	Dimensions of Wheal in Cm.	Serum Calcium, Mg. in 100 C.c.	Serum Phosphorus, Mg. in 100 C.c.	Date of Calcium and Phosphorus Determination
98	12	1/28/25	7,600	1 × 1.0 1 × 1.2	4.9	7.6	1/27
		2/17/25	8,100	1.1 × 1.2 1.0 × 1.4	7.0 7.7	5.9 5.4	2/14 2/19
		2/25/25	8,100	1.1 × 1.2 1.1 × 1.1	9.7	4.5	2/26
		3/14/25	7,900	1.0 × 1.1 1 × 1.3			
96	8	1/21/25	6,600	1.0 × 1.5	6.2 6.7	5.9 4.6	1/17 1/23
		1/28/25	.....	1.1 × 1.1 1.2 × 1.1	8.7	5.5	1/28
		2/25/25	7,400	1.1 × 1.5 1.2 × 1.5	10.1	5.6	2/19
6	15	12/ 4/23	7,850	1.0 × 1.2	9.9	4.7	12/ 3
8	15	12/ 4/23 1/24/24	6,750	1.2 × 1.3 1.1 × 1.0	9.5 9.7	3.5 3.4	11/26 1/17
84	11	12/ 4/23	6,000	1.0 × 1.0 1.1 × 1.1	9.7	1.8	
52	5	3/29/24	5,800	1.0 × 1.3	11.3	5.8	3/ 5
43	17	3/15/24	8,750	1.2 × 1.3	10.9	3.5	3/12
36	24	2/29/24	8,950	1.0 × 1.4	9.9	3.5	2/29

the mean being 7.3 mg. In these subjects, also, there was no indication that the low calcium content had any influence on the vessel permeability; the wheals all fell within the limits of those in subjects with normal serum calcium. There was neither increased nor decreased sensitivity of the skin to minimal codein solutions (1:1,000,000) in fourteen experiments.

One negro infant gave such an unusually marked reaction that it was not included in the foregoing series, although the serum calcium was low. The serum calcium was 6.8, 5.8 and 6.2 mg., at intervals from one to two weeks; the serum phosphorus was normal (from 4.6 to 5.1 mg.) and the blood sodium on one occasion was normal (3.18 mg. per hun-

dred cubic centimeters). On three separate days wheal formation was marked, the wheals varying from a minimum of 1.3 by 1.6 cm. to 1.7 by 2.0 cm., with more than the usual induration, and a disappearance time prolonged from one to more than two hours. Aside from the low serum calcium and associated rickets and spasmophilia, no abnormalities were present. The child left hospital before the serum calcium became normal, so that it is not definitely known whether the low calcium was a factor in causing the unusual vascular permeability; however, another subject with approximately normal calcium gave a similar wheal reaction, so that it is not probable that the low calcium was a causative factor in the reaction.

The Relation of the Blood Calcium and Sodium to Wheal Formation.—It has been stated [7] that normal vessel permeability is related to the proper balance between the calcium and sodium content of the blood; an excess of sodium increasing vessel permeability and of calcium decreasing it. In this work there were no subjects with an excess of blood sodium, but as there were several with the normal amount of sodium and a decreased amount of calcium a relative preponderance of sodium was present; and later when the calcium had reached the normal level, there was the normal relation between these ions. In four such subjects (with serum calcium of 6.2, 6.5, 6.9 and 7.1 mg. per hundred cubic centimeters) there was no indication that a relative sodium ion preponderance increased vessel permeability as measured by the codein wheal formation. It happened that in three instances the wheal formation was the same, with relatively greater sodium content and somewhat less in the fourth, but the difference was of no account. While this work was in progress, the blood sodium percentage was determined in about thirty infants and young children in the pediatric laboratory, and in no case was the percentage materially below the normal; it is probable then, that the patients in the low calcium series also had approximately normal blood sodium content, and, as we have seen, the low serum calcium does not modify the wheal reaction, it is presumably evidence that the relative sodium preponderance was without effect on the wheal reaction.

PHOSPHORUS

Variations in the phosphorus content of the serum had no demonstrable effect on the wheal reaction; the phosphorus determinations were made together with those of calcium, so that there were various combinations of low, normal and relatively high phosphorus contents with low and normal calcium content. Normal serum phosphorus and calcium percentages were considered to be 5.0, and from 10 to 11 mg. respectively

7. Loeb, J.: J. Biol. Chem. **23**:423, 1915.

per hundred cubic centimeters of serum. In none of these combinations were there demonstrable departures of the wheal reaction from the general average. There was no example of a very low phosphorus percentage with normal calcium, but several experiments with the subjects' serum phosphorus varying from 2.3 to 3.5 mg. and serum calcium from 7.3 to 8.0 mg. gave average reactions. In a single subject as the phosphorus increased from 2.3 to 4.2 mg. (and calcium from 7.9 to 9.9 mg.) the reactions were the same. Without change in the wheal reaction in one experiment, the phosphorus and calcium increased from a relatively low level (4.0 and 6.9 mg. respectively) to a relatively high phosphorus (6.4 mg.) and a normal calcium content (10.4 mg.). Further, the reaction was the same in another subject as a combination of what may be considered a relatively high phosphorus (7.6 mg.), and low calcium content (4.9 mg.) changed to a phosphorus content possibly a little below normal (4.5 mg.) and an approximately normal calcium content. In view of these results, the conclusion is justified that variations in the phosphorus content of the serum from a low to a relatively high level have no influence on the codein wheal reaction.

CONCLUSIONS

Low serum calcium and phosphorus, down to half the normal quantity, in infants with rickets or spasmophilia have no influence on the permeability of the minute vessels of the skin, as measured by the codein wheal reaction.

News and Comment

DEATH OF DR. JAMES STEWART FOWLER

Dr. James Stewart Fowler, one of the editors of the *Edinburgh Medical Journal* for the past thirteen years, died in Scotland, in August, 1925. He had been associated with Dr. John Thompson and other members of the staff of the Edinburgh Sick Children's Hospital, and was considered an authority on pediatrics. He lectured on diseases of children at the University. His writings include "The Action of Red Bone Marrow and Other Substances on the Regeneration of the Blood and on the Splenic Anemia of Infancy," a handbook on "Diseases of Children" by Fowler and Elder, a book on "Artificial Feeding of Infants," and many contributions to encyclopedias and medical journals. He is the author of a recent communication on the subject of erythrodema, which has been abstracted in this journal.

Correspondence

FEVER IN NEW-BORN INFANTS*

To the Editor:—In a recent paper, read before the American Pediatric Society and published in the *American Journal of Diseases of Children*,[1] considerable space was devoted to a discussion of results reported by my co-workers and myself[2] on the nature of fever in new-born infants. We found (1) that the serum protein concentration, determined refractometrically, is considerably higher in febrile than in afebrile new-born infants, indicating, probably, a loss of water from the serum; (2) that the administration of fluids by mouth causes a simultaneous fall in temperature and blood concentration as measured by the change in serum protein concentration and red blood cells. From these findings we conclude that fever in new-born infants is due to dehydration.

Sherman objects to our conclusions on the basis that "this method (the refractometric) assumes that the serum proteins are present in the blood in the same concentration normally and during inanition fever. Hence any variations which occur in the febrile cases are not due to actual changes in the amount of proteins present, but to addition or subtraction of the water." This statement is not altogether clear. Apparently, Sherman, in the first sentence, means total serum protein $\left(\frac{\text{Plasma volume c.c.} \times \text{serum protein per cent.}}{100}\right)$. The question as to whether the change in serum protein concentration denotes a change in total fluid or in total plasma protein cannot as yet be answered definitely. It seems probable that the increase in plasma protein concentration in a starving infant is due to a loss of fluid from the plasma rather than to the building up of new plasma protein. An association between fever and increased plasma protein concentration has also been recently noted by Schiff[3] and his co-workers during experimentally induced dehydration.

Sherman further states: "Bakwin and his collaborators have not included, in their published papers, the actual determinations of serum proteins in normal infants as compared to those suffering from dehydration fever." In the paper, "Dehydration in New-Borns,"[2] a figure is shown with the results in 124 afebrile new-born infants.

Sherman raises another objection: "Secondly, in order that the refractometric method be accurate, the assumption must also be made that the other constituents of the blood plasma do not vary greatly under the imposed experimental conditions." He points to "large increases in concentration of urea and amino-acids" and says: "These factors must be taken into consideration if refractometric determinations are to be of the greatest value." The large increases in amino-acids are not evident in the published table of Sherman and his co-workers. In every instance in which comparative determinations

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*A reply to Sherman, Pucher and Lohnes.

1. Sherman, D. H.; Pucher, G. W., and Lohnes, H. R.: Blood Chemistry of the New-Born in Health and in Inanition Fever, Am. J. Dis. Child. **30**:496 (Oct.) 1925.

2. Bakwin, H., and Goss, C.: Dehydration in New-Borns, I. Am. J. Dis. Child. **24**:497 (Dec.) 1922. Bakwin, H.: Ibid. II. **24**:508 (Dec.) 1922. Bakwin, H.; Morris, R. M., and Southworth, J. D.: The Effect of Fluid on the Temperature and Blood Concentration in the New-Born with Fever, Am. J. Dis. Child. **27**:578 (June) 1924.

3. Schiff, E.; Eliasberg, H., and Bayer, W.: Zur Pathogenese der Ernährungsstörung beim Saugling, Jahrb. f. Kinderh. **106**:263 (Aug.) 1924.

were made, the amino-acids were lower on the third day during the fever than on the first day. Sherman gives as his average for febrile babies 12.46 mg., as against 7.45 for afebrile new-born infants. In obtaining his average for febrile babies he has given his one determination of 36.3 mg., the same value as his others. Miss Helen Rivkin has determined for me the changes in the refractive index due to various concentrations of urea. The error caused by an increase in the urea nitrogen from 15 to 75 mg. per cent. (a much greater increase than found in any of Sherman's cases) amounts to less than 0.009 per cent. of protein. (According to Sherman, 7 per cent. was well within the limits of error of his method of determining total solids.)

Sherman discusses blood volume determinations reported by Rivkin and myself.[4] He is apparently surprised to find that in infants between the ages of 2 and 4 months, "Bakwin's data show no appreciable change in blood volume (0.3 per cent.), while the estimation of serum proteins indicates a marked blood concentration (6.36 per cent.)." We should hesitate to call an increase of 6.36 per cent. in the serum proteins marked. The normal fluctuation, as for urea, sugar, etc., is fairly wide, and it is only when large variations occur that conclusions can be drawn, particularly when different children are compared. As Sherman points out, the average increase in the serum protein concentration found by us in new-born infants with fever was 30 per cent. We do consider such an increase of significance.

Sherman raises another objection: "In our experiments, the total water content of the blood was calculated from the total solids. This, of course, is only a very rough index of blood concentration. Nevertheless, if Bakwin's refractometric data are taken as standards, the dehydrated babies should show a very marked increase of total solids, an average of 30 per cent., with a minimum of 7 per cent." The discrepancy between our results and those of Sherman and his co-workers is not at all surprising when the difference in methods is considered. Fluctuations in serum protein concentration measure variations in plasma water per cent.; the total solids, made up largely by hemoglobin from the red blood cells, indicate variations in whole blood water. A reduction of the plasma fluids by one-half would cause a 100 per cent. increase in the serum protein concentration (unless there was protein destruction); while in whole blood, with a cell volume of 50 per cent., the total solids would be increased only about 30 per cent. The greater the cell volume, the greater the discrepancy. In new-born infants, the cell volume is usually over 50 per cent. and often over 60 per cent. Furthermore, it is probable that the hemoglobin content of the blood of new-born infants varies markedly during the first few weeks of life, independent of changes in blood water.

Sherman concludes his paper with the following statement: "In general, the foregoing data have a tendency to indicate that the changes in blood volume are in the direction of increased water addition to the blood, which is not inconsistent with the blood chemistry findings." He bases this statement on the fact that his average blood water per cent. in babies without fever was 79.1 per cent., while his average for babies with fever was 79.69 per cent. Seven per cent., Sherman states, was well within the limits of error of his method. The difference which he found between afebrile and febrile babies was approximately 0.8 per cent. It is of interest to note that in four of the six cases in which comparative observations were made, Sherman and his co-workers found the percentage of water in the blood decreased during the fever.

1022 Park Avenue.

HARRY BAKWIN, New York.

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4. Bakwin, H., and Rivkin, H.: The Estimation of the Volume of Blood in Normal Infants and in Infants with Severe Malnutrition, Am. J. Dis. Child. **27**:340 (April) 1924.

Abstracts from Current Literature

Anatomy and Physiology

THE DETERMINATION OF BLOOD GROUPS IN TWINS. A. F. CANELLI, Clin. Pediat. **7**:385-395, 1925.

Twins of a single chorion belong to the same blood group; twins of a double chorion may, and usually do, belong to different groups.

The determination of the blood groups is not a positive indication that the twins are of monochorion origin, however, since many bichorion twins show the same blood classification. Associated with other points of identification, its value is considerably increased.

THE EFFECTS OF CHOLESTERIN ON THE ERYTHROPOIETIC SYSTEM. G. HALFER, Clin. Pediat. **7**:425-428, 1925.

A single dose of cholesterin (by mouth) produced a transitory increase in the number of red blood cells.

Prolonged oral administration of the drug resulted in a primary decrease, and after eight months, in a permanent increase, in the number of red cells. The resisting powers of the erythrocytes were also increased.

No toxic effects from the cholesterin were observed.

ZAMBARANO, Northville, Mich.

INVESTIGATIONS CONCERNING THE FREE OR COMBINED CONDITIONS OF GLUCOSE IN THE BLOOD. CHRISTEN LUNDSGAARD and SVEND AAGE HOLBOLL, Ugesk. f. Laeger **40**:865, 1925.

These authors come to the unqualified conclusion that the glucose in the blood of patients suffering from diabetes mellitus, exists in a free, crystalloid and diffusible form. While diffusion is slower from blood than pure glucose solutions, it is only a quantitative not a qualitative change of the glucose, and depends probably on cellular contents of the blood. Glucose added to blood diffuses with the same readiness as the preexisting glucose of the blood.

SCHLUTZ, Minneapolis.

Pathology, Bacteriology and Biochemistry

COMPENSATORY HYPERTROPHY OF THE THYMUS GLAND IN THE RAT. J. MARMORSTON-GOTTESMAN and HENRY L. JAFFE, J. Exper. Med. **42**:413, 1925.

The right lobe of the thymus was removed under ether anesthesia. At necropsy at a later date, the weight of the remaining left lobe was compared with that of the corresponding lobe of a litter control of the same sex, with the following results: In five rats under puberty, at necropsy fifteen days after lobectomy, the remaining (left) lobes averaged 37 per cent. in weight above the left lobes of the controls. The average difference between the weight of the right and left lobes of the controls was only 3 per cent. The difference between the body weights of the controls and experimental rats was only 1 per cent. In another group of four rats, a little younger, killed

from three to four weeks after operation, the remaining (left) lobes averaged 42 per cent. heavier than the left lobes of the normal controls. No compensatory enlargement of the remaining lobe of the thymus was found in rats in which lobectomy was done after puberty.

According to the authors, the results clearly indicate that uncomplicated compensatory hypertrophy of the remaining lobe occurs after removal of one lobe of the thymus in young rats, and the results emphasize the functional importance of this gland before puberty.

McClure, Evanston, Ill.

Electro-Endosmosis Through Mammalian Serous Membranes. II. Comparison of Hydrogen Ion Reversal Points with Acetate and with Citrate-Phosphate Buffers. Stuart Mudd, J. Gen. Physiol. **9**:73 (Sept.) 1925.

The author has shown in a previous study that the endosmotic current of fluid passing through a serous membrane which is subjected to an electric current reverses its direction at a certain p_H. This hydrogen ion concentration at which reversal takes place is determined not only by an inherent characteristic of the membrane itself but also by the nature of the buffer in which it is bathed. The monovalent anion acetate buffers gave a reversal at a point almost one half a p_H unit more alkaline than the polyvalent anion citrate buffers. It is believed that the acetate values more nearly correspond to the true hydrogen ion reversal points, because the blood buffers contain polyvalent ions in only very small amounts.

Hoag, New York.

Experimental Investigations Concerning the Double Effect of Calcium on the Vegetative Nervous System. E. Barath, J. Nerv. & Ment. Dis. **62**:661-664 (Sept.) 1925.

The thesis by Kraus and Kondek, stating that alterations of vegetative nerve activity are analogous to the effect of certain cations, furnishes the basis of calcium experimentation in man by the author, since calcium salts are entering the clinical field more widely.

Morning experiments were made on hungry persons following preliminary tests of epinephrin mydriasis, Aschner's test, blood picture and sugar, pulse, blood pressure and pupil tests. Patients were given intravenously 5 c.c. of a 10 per cent. solution of calcium chlorid, and after ten days 10 c.c. Duration of injection was from thirty to forty seconds. Features of the results are: Immediately after and sometimes during injection there was a slowing of the pulse to as low a rate as 35 to 15 per minute. In some cases a rate of from 50 to 45 per minute was observed. Aschner's test becomes positive. If positive beforehand, it is increased. Blood sugar rises a little. Blood pressure may increase from 10 to 20 mm., often preceded by an initial depression. After from five to ten minutes, the pulse rate becomes normal and Aschner's test is negative. If 0.0005 gm. of atropin sulphate is given by injection before the calcium, slowing of the pulse does not appear. From 0.0001 to 0.0002 gm. given intravenously at the height of bradycardia will bring about a normal rate. The author maintains that in man the calcium effect shows an initial vagus excitement of short duration, followed by a longer period of weaker sympathetic excitement.

Floyd, Iowa City.

ALKALI BINDING CAPACITY OF THE BLOOD SERUM. J. CSAPO and S. HENSZELMAN, Orvosi hetil. **69**, 1925.

The acid binding capacity of the blood serum was determined with electrometric methods. In healthy children 100 c.c. of serum with 1 per cent. of protein is able to bind, beside the already fixed alkali, on the average about 100 c.c. of hundredth normal sodium hydroxid.

In tuberculosis and pleurisy, the amount of alkali per 1 per cent. of protein decreases. The alkali binding capacity of the serum, therefore, is less than the acid binding capacity. The cause of this is that the alkali binding capacity of the serum proteins is already exhausted by the original alkali content, and so addition of alkali will not increase the amount of fixed alkali to the same extent as addition of acid does that of fixed acids.

ALKALI CONTENT OF THE BLOOD IN HEALTHY AND SICK CHILDREN. J. CSAPO, Orvosi hetil. **69**:659, 1925.

Csapo devised a new method for the determination of alkali content of the blood. In healthy children 1 c.c. of blood serum contains on average an amount of alkali equivalent to 4.8 c.c. of $\frac{N}{100}$ sodium hydroxid; 1.4 c.c. of this falls to free alkali, 3.4 c.c. to alkali bound to proteins. The alkali content of the blood serum changes according to protein content. In 100 c.c. of serum 1 per cent. protein corresponds with 30 c.c. of fiftieth normal, or 60 c.c. of hundredth normal sodium hydroxid. This figure is named as an alkali-protein quotient. Of diseases, tuberculosis shows a decrease of alkali and of the alkali-protein quotient.

ACID BINDING CAPACITY OF THE BLOOD IN HEALTHY AND SICK CHILDREN. J. CSAPO and G. MIHALOVICS, Orvosi hetil. **69**:681, 1925.

The acid binding capacity of blood and plasma was determined, and also the relation of plasma to cell elements with hematocrit methods. In healthy children, 1 c.c. of blood binds from 14 to 15 c.c., 1 c.c. of plasma, 7 c.c. of fiftieth normal acid. The acid binding capacity of the blood is about twice that of the plasma, and it increases or decreases with the red blood cell content. From the acid binding capacity of blood and plasma and the relation of plasma cell elements, the amount of fixed acid per volume per cent. of red blood cells may be figured out. This corresponds to 0.27 to 0.31 c.c. of fiftieth normal acid. This figure is named acid-red blood cell quotient. In acute and chronic febrile diseases the acid binding capacity, as well as the quotient showed a decrease in a number of cases. In combined cases of severe anemia with jaundice, the total acid binding capacity is low, while that of the red blood cells is high, and so the acid red blood cell quotient increases above normal.

ZENTAY, St. Louis.

Nutrition

THE CONTROL OF RICKETS. MARTHA M. ELIOT, J. A. M. A. **85**:656 (Aug. 29) 1925.

That animals can be protected against rickets by the use of cod liver oil and ultraviolet light is an established fact. It has also been clearly shown that cod liver oil and sunlight exert a great influence in the cure of rickets Whether these measures are sufficient to prevent rickets in infants in a community has been made a problem of investigation by the author, who describes the plan of the study and offers a preliminary discussion of the results. These investigations have shown that a slight degree of early rickets is well nigh

universal in our climate and in our state of society. The very intimate association of rickets with growth, its early appearance regardless of season, and its universality raise the question whether this slight degree of rickets must not be considered normal. That rickets is intimately associated with growth is well known, and that it should appear at the time when most active growth is taking place, namely, the first four months of life, is not extraordinary. The rate of growth of the infant influences the early development of the disease. Large, rapidly growing breast-fed infants and very fat infants uniformly show definite evidence of rickets. It is an uncommon thing to find a healthy, vigorous breast-fed infant who does not show rickets by roentgen-ray examination. Premature babies, who grow exceedingly rapidly, are notoriously rachitic. Malnourished infants frequently show small, slender bones with little or no rachitic change. If any two groups of infants show the need of early antirachitic treatment more than others, they are the large, rapidly growing breast-fed infants and the premature infants.

UNIVERSALIZING BREAST FEEDING IN A COMMUNITY. FRANK HOWARD RICHARDSON, J. A. M. A. **85**:668 (Aug. 29) 1925.

The author states that to universalize breast feeding in a community, the procedure must consist of several essentials. There must be a group of physicians who are convinced of the overwhelming superiority of breast feeding, who believe it attainable for the vast majority of infants, and who are familiar with a working technic for making breast feedings possible for the individual child. There must be cooperation of the birth recording department of each community, and there must be an organization controlling sufficient nurses trained in the technic of breast feeding to visit each new mother in order to instruct her in the desirability of keeping her baby on the breast, as well as in the way to accomplish this. The first large scale piece of work of this sort was done in Nassau County, New York. The infant mortality rate during the year of active campaign was sixty-four per thousand while that of the three years preceding the experiment averaged seventy-two.

BONAR, Salt Lake City.

CLOSTRIDIUM MULTIFERMENTANS IN CHOCOLATE CREAM CANDIES. GRACE A. HILL, J. Bacteriol. **10**:413, 1925.

The author presents evidence of the presence of a saccharolytic anerobe in cracked chocolate creams. This organism is classified tentatively as *Clostridium multifermentans* (Stoddard). Of twenty-four samples of spoiled chocolate creams examined, eighteen showed the presence of gas producing organisms.

The "mazetta," used as a foundation for cream fillings, was found to contain the organism in several instances. It could be isolated also from egg albumin, which in turn is the foundation for mazetta cream.

It had been observed that apparently good candies from batches having cracked candies were usually found to contain *Clostridium multifermentans*. At no time was the organism found in candies from batches showing no spoilage.

WESTLUND, Chicago.

INCIDENCE OF RICKETS IN THE BREAST-FED INFANT. GEORGE J. MOHR, Northwest Med. **24**:430 (Sept.) 1925.

Mohr considers (1) that breast feeding does not entirely protect the child from rickets; (2) that rickets occurs less frequently in the breast fed than in the artificially fed; (3) that antirachitic measures should be routine in the feeding of all infants.

SCOTT, Philadelphia.

STUDIES ON GASTRO-ENTERITIS IN INFANCY. A. CANELLI, Pediatria **33**:876, 1925.

Canelli uses a pathologic classification and divides gastro-enteritis in infancy into two groups. 1. Gastro-enteritis with degenerative changes in the organs, parenchymal hemorrhage and gastro-intestinal hemorrhages. 2. Gastro-enteritis without any pathologic changes and without hemorrhages.

Canelli studied 100 cases of cholera infantum and found blood in the stools, vomitus and often in the urine of these infants. There was no biliverdin in the stools of most. In the grave cases, the excess of uric acid in the urine paralleled the progress of the toxic syndrome and the diminution of the amount of urine passed. Intertrigo about the thighs and buttocks was present almost constantly, and was caused by the marked acidity of the stools and urine. Acetone and indican were frequently present, as was albumin; in severe cases, the urinary findings were those of an acute nephritis. Leukocytosis was noted and especially so in the severe cases. Canelli places cholera infantum in the first group of his classification and believes that the condition is a definite clinical entity.

DE SANCTIS, New York.

PHYSIOLOGY AND PATHOLOGY OF GASTRO-INTESTINAL DISTURBANCES IN INFANCY. P. ROHMER, Rev. franç. de pediat. **1**:73, 1925.

In this review, Rohmer offers a critical study of the different systems of classification of disturbances of the gastro-intestinal tract in infancy, with particular emphasis on the underlying physiologic pathology. He feels that in order to understand the advances made in this field, there should be an agreement on the use of terms as well as on the clinical entities. Although admitting that digestive disturbances in the infant have a greater effect on life processes beyond the intestinal barrier than they do in an older individual, he feels that the use of the term "nutritional disturbances" to include all pathologic modifications of growth processes (aside from anomalies) is too vague and too extensive a one to be of much value in a system of classification. He prefers the general heading of "Disturbances of the Digestive Tract and of Nutrition in Infants"; and under this he discusses (1) The alimentary dystrophies, (2) the dyspepsias, (3) the choleriform syndrome and (4) athrepsia.

LESLIE, Chicago.

HYDROGEN-ION CONCENTRATION OF THE BLOOD IN INFANTS WITH ATROPHY AND DYSPEPSIA. Z. BOKAY, Orvosi hetil. **69**:635, 1925.

Hydrogen ion concentration of the blood of infants with atrophy and dyspepsia gives normal or slightly acidotic values. Atrophy (athrepsy) is not necessarily combined with acidosis, it only predisposes to it. In very severe cases of atrophy, the hydrogen ion concentration may be entirely normal. Marked alkalosis was seen only in a case of pyloric stenosis probably due to loss of acids through persistent vomiting.

ZENTAY, St. Louis.

PATHOGENESIS OF NUTRITIONAL DISTURBANCES IN INFANTS. V. THE KIDNEY SYNDROME: DEHYDRATION PYURIA, CYLINDRURIA AND ALBUMINURIA. E. SCHIFF and W. BOYER, Jahrb. f. Kinderh. **108**:157, 1925.

In an earlier communication, the authors reported the experimental production of a slight albuminuria, pyuria, and cylindruria in infants and even in some, mild hematuria, by marked reduction of their fluid intake. This being

exactly the kind of urinary findings noted frequently in intoxication and in other severe nutritional disturbances accompanied by great loss of fluids, they conclude that an intimate relationship must exist between water impoverishment of the body and the appearance of pathologic elements in the urine. This contention is substantiated by the fact that the kidney syndrome disappears when fluids are again administered in sufficient quantities, just as does the so-called dehydration fever. The authors have previously shown that thirst fever was only observed when they were able to cause anhydremia, and that anhydremia was only produced if the food given in their thirst investigations contained protein. By experimenting with diets containing protein and with diets practically free from protein, in which the water had been reduced to 40 to 50 per cent. of the normal requirements, they found that the kidney symptoms appeared entirely independent of the nature of the food elements and of the presence or absence of anhydremia. The kidney syndrome is due to the reduced water intake alone. Abnormal conditions in the blood and blood vessels disturb the kidney function. Reduction of the amount of blood flowing through the kidney means a disturbance of oxygen metabolism; the oxygen needs of the kidney are high as compared to other organs, and this is especially true in infants. Whether the injury to kidney cells is produced by decrease of oxygen or increase of carbon dioxid is not clear. A decreased alkali reserve in the blood has been produced by experimental dehydration, and we know that an acidosis is present in severe cases of intoxication. The true pathogenesis of the kidney syndrome is not yet clear. The kidney syndrome is a residual symptom of a water impoverishment of the body of varying intensity, and due to various etiologic factors. These cases are designated dehydration pyuria.

Clinically, we designate two types of pyuria; first, that type with severe general symptoms in which at necropsy there is either a diffuse round cell infiltration with tendency to softening of the tissues of abscesses of various sizes in the kidney cortex; and, secondly, that type in which the pyuria is found only accidentally and unaccompanied by any symptoms of acute illness. In this latter type, if the child died from some intercurrent infection such as pneumonia following a condition of severe dehydration, the pathologic findings would be the same as those found in babies dying of intoxication, that is, fatty changes in the kidney epithelium, especially in the tubuli contorti.

The authors conclude that dehydration pyuria comes first, evidencing an injury to the kidney which produces a locus minoris resistentia, and if bacteremia is present, either in the primary condition which produced the dehydration pyuria, or as a later complication, then true pyelitis supervenes. These arguments would substantiate the hematogenic origin of pyelitis, and would make it appear improbable that an ascending infection is of great significance. Colon bacillus, they contend, must be of secondary importance and not the causative organism.

PARMELEE, Chicago.

THE QUESTION OF GOAT'S MILK ANEMIA IN INFANTS. H. BRUNING and W. FISCHER, Med. Klin. **21**:12, 1925.

It is a well known fact that infants fed on goat's milk are apt to develop anemias of a severe form. The authors have observed three cases of severe anemia in infants from 7 to 8 months of age. In one of the cases the hemoglobin was as low as 13 and the red blood cells 428,000, with a color index of 1.6.

The pathogenesis of this anemia is not quite clear. The investigators of the problem tried to explain it on the basis of improper feeding of the goats

and an anemia of the animals themselves, also with avitaminosis of the milk and hemolytic effect of the milk due to fatty acids of a high molecular composition. Undoubtedly, there is also a constitutional factor, which is responsible, as the anemia develops in only a comparatively small number of infants. The problem needs further study.

ZENTAY, St. Louis.

STUDIES OF THE ACID-BASE RELATIONS IN THE CHILD. A. HOTTENGER, Monatschr. f. Kinderh. **30**:497, 1925.

The writer has made a rather extensive study of the excretion of organic acids in infancy and in childhood. The technic used was that employed by Van Slyke and Palmer. He submits many charts of his analyses and also describes the details of the method. His conclusions are as follows:

1. The excretion of organic acids in the urine is rather constant in amount. It is somewhat higher in the growing organism than in the adult. Premature children and young nurslings excrete for every kilogram of weight about 10.1 c.c. of acid, while in thriving babies, bottle fed, and older ones breast fed, the amount is about 12.5 c.c. In the adult it is 8.2 c.c.

2. Young nurslings which thrive on a minimum of protein show an increase in excretion with an increase of protein in the diet. In older children, high or low protein has no effect. Twenty per cent. cream added to breast milk, that is, high fat and low protein, as well as high carbohydrate and high protein lower the values. A twenty-four hour fast decreased the excretion in a well baby, while it caused an increase in a hungry infant.

3. Acids given by mouth cause varying results. Large amounts of citric acid are burned in the body up to 95 per cent. Lactic acid increases the excretion.

4. Organic acids and their salts alkalinize the urine by withdrawing alkali from the body.

5. There is little relation between the organic acid excretion and that of phosphate and ammonia.

6. A total phosphate determination gives little insight into the amount of acid excreted and certainly is of no value in estimating whether the acid is organic or inorganic.

7. There is a relationship to mineral metabolism. Calcium chlorid increases excretion. Citrates seem to cause elimination of phosphate in the urine.

8. The excretion of organic acid is increased in starvation, fever, pyelitis, infantilism, rickets, and in some stages of spasmophilia. It is lowered in the hunger period used for treating acidosis and diarrheas, in some burns and in manifest tetany. It is unchanged in eczema and in chronic febrile conditions.

9. The writer believes that the liver plays a large part in the metabolism of organic acids.

10. Most of the organic acid formed in the intermediary metabolism comes from the protein.

THERAPY OF RICKETS. S. ROSENBAUM, Monatschr. f. Kinderh. **30**:547, 1925.

This study was made to determine the effects of different remedies on the course of rickets. The children ranged in age from 12 to 20 months. The progress of the disease and the result of therapy were determined by the

roentgen ray. The patients were kept in the same room, and with the exception of a special out-of-doors group used as a control, did not leave this room. All were kept on the identical diet.

Of all remedies tried, none had any effect whatsoever except real and artificial sunlight.

The writer asked the question whether the effect of the light treatment might be indirect from the irritation of the skin. Irritation of the skin, however, by mustard baths, massage and salt rubs, did not influence the disease.

To test whether the healing element in light can be transmitted by the blood, he submitted blood to two minutes' exposures and then injected it in doses of 5 c.c. Twenty-eight such inoculations had no effect on the course of the rickets.

GERSTLEY, Chicago.

Diseases of the New-Born

NEONATAL PYELITIS. L. W. SAUER, J. A. M. A. **85**:327 (Aug. 1) 1925.

This brief clinical report on neonatal pyelitis is based on fifteen cases. It is submitted because: (1) the disease occurs periodically and may be easily overlooked; (2) the early symptoms are invariably referable to the gastro-intestinal tract or to the central nervous system, and (3) its occurrence at such an early age in a preponderance of male infants may shed some light on the route of the infection. Microscopic examination and culture of the urine of fifteen nonthriving new-born infants with gastro-intestinal symptoms or cyanosis revealed pus and *B. coli* in fourteen instances. When free from complications, the disease usually responded within six weeks to diuresis and continued alkalization of the urine. The infection is probably due to pathogenic, enteral *B. coli* which localize by way of the blood stream.

INTRACRANIAL HEMORRHAGE IN THE NEW-BORN. CLIFFORD G. GRULEE, J. A. M. A. **85**:336 (Aug. 1) 1925.

The author feels that in the present state of our knowledge, the best treatment for intracranial hemorrhage is absolute quiet and rest; that the measures up to the present time adopted for the relief of the condition are satisfactory neither from the theoretic nor from the practical standpoint; that the damage is done before the measures can be of value, and that, as a consequence, until a diagnosis is made much earlier than it seems at present possible, the best plan to be followed is to see that nothing is done to disturb the quiet of the infant.

THE SPINAL FLUID IN THE NEW-BORN. M. HINES ROBERTS, J. A. M. A. **85**:520 (Aug. 15) 1925.

The author performed a lumbar puncture on 423 negro babies as soon after delivery as possible. The great majority of the fluids were obtained within the first twenty-four hours, subsequent punctures being done on many of these patients about the ninth day of life, and a few were done again as late as the fourth week. Each of these fluids contained a yellow pigment, bilirubin, which persisted at least until the ninth day and was intensified after jaundice occurred. It cleared up by the fourth week. The intensity of pigmentation was closely related to the physical development of the child. Sixty cases, or 14.1 per cent., showed the presence of intracranial hemorrhage, two due to hemorrhagic disease, and fifty-eight to trauma. Abnormal labors or opera-

tive procedures tend to increase the incident of intracranial disease. Prematurity is a definite etiologic factor. Only twenty-six of the sixty cases presented symptoms attributable to intracranial hemorrhage. Of fifty-four of the sixty children followed: twelve are dead, ten of these died as the result of hemorrhage and two as the result of some intercurrent infection. Of the forty-two remaining children, only two showed symptoms due to hemorrhage. The author concludes from his study that xanthochromia of the spinal fluid of new-born infants is a physiologic condition, in no way dependent on the existence of hemorrhage or other pathologic conditions of the nervous system. Intracranial hemorrhage in the new-born is of common occurrence even in normal labor, and only in severe cases does it exhibit symptoms. The death rate is high. Death occurs very shortly after birth in those cases terminating fatally. The possibility of later and permanent disability resulting from intracranial hemorrhage seems remote.

UMBILICAL HEMORRHAGE ACCOMPANIED BY DEEP JAUNDICE. HONORIA ACOSTA-SISON, J. A. M. A. **85**:1201 (Oct. 17) 1925.

The author reports a case occurring in a baby, aged 20 days. The cause of hemorrhage and jaundice could not be ascertained. The child died of exsanguination at the age of 1 month and 22 days. The jaundice appeared soon after birth and gradually grew in intensity until death. No improvement was noticed as a result of roentgen-ray treatment. The coagulation time and the platelet count were not determined, but the blood that had oozed and had been undisturbed for more than seven hours was found to be liquid. After each transfusion, bleeding of the umbilicus was practically stopped and at the end of from four to five days the bleeding recurred. Finally, diffuse bleeding from the mucous membranes of the mouth and intestines occurred. The bleeders in the family of this infant were on the father's, not on the mother's side. The father's Wassermann reaction was negative and the obstetric history of the mother presented no indication of syphilis.

BONAR, Salt Lake City.

FAMILIAL ICTERUS GRAVIS OF THE NEW-BORN AND ITS TREATMENT. A. P. HART, Canad. M. A. J. **15**:1008 (Oct.) 1925.

In the family history, the birth of six boys and one girl were reported. The six boys were all apparently normal at birth but all developed jaundice within twenty-four hours and died within three to eleven days. The girl also was severely jaundiced for a year following birth, and did not gain in weight but she ultimately recovered. The present baby developed jaundice within twenty-four hours of birth but was normal otherwise. The jaundice increased markedly in intensity.

Physical examination was normal except for the intense jaundice. The blood count and fragility test were normal. The direct van den Bergh test was negative; the indirect test was strongly positive. Bile was found in urine and bowel movement.

The etiology of the condition is not known. The author discusses the various theories of sepsis and toxemia. The treatment in this case consisted of an exsanguination transfusion; 300 c.c. of blood was removed from anterior fontanel, at the same time transfusing 335 c.c. of blood into the internal saphenous vein at the left ankle. Sixty cubic centimeters of 5 per cent. glucose solution was also given.

The jaundice rapidly disappeared and the baby made an uneventful recovery.

An excellent bibliography is attached to this article.

MOORE, Omaha.

PROPHYLACTIC LAVAGE IN NEWLY BORN. E. SLAWIK, Med. Klin. **21**:163, 1925.

Prophylactic lavage of the stomach is advisable in cases in which swallowing of amniotic fluid may be supposed, i. e., in babies born with intra-uterine or postnatal asphyxia. Through this method we prevent vomiting and its consequences and so help the starting of normal functions of the gastro-intestinal tract. It is strictly indicated in cases with foul smelling, infected amniotic fluid. Here the method means a prevention of septic infection of the gastro-intestinal tract. The method is without any danger even at this early age.

ZENTAY, St. Louis.

Acute Infections

SMALLPOX OCCURRING IN TWINS AT BIRTH. JAMES M. MARTIN, J. A. M. A. **85**:268 (July 25) 1925.

The mother, while in the second stage of a very severe attack of smallpox, gave birth to twins, both of whom were in the papular stage of the disease. The mother recovered and the prognosis for the infants was good.

DOES ROENTGEN RAY MODIFY THE COURSE OF WHOOPING COUGH? HAROLD K. FABER and HOMER B. STRUBLE, J. A. M. A. **85**:815 (Sept. 12) 1925.

In two parallel series of cases of whooping cough, selected mainly by alternation, one group treated by roentgen ray and the other by antipyrin, the disease ran an average longer course, fewer patients ceased whooping in the early weeks and more patients were still whooping in the late weeks in the irradiated series than in the controls. The present study would appear to justify the conclusion that radiotherapy is without true beneficial effect in pertussis. The occasional temporary exacerbations or inhibitions of attacks following roentgen-ray therapy should probably be ascribed to psychic disturbances. Effects of greater extent or duration, such as have been previously reported from roentgen ray as from other modes of treatment, are in all probability apparent rather than real and represent normal fluctuations in the course of a highly variable disease.

THE TREATMENT OF THRUSH WITH GENTIAN VIOLET. HAROLD K. FABER and LLOYD B. DICKEY, J. A. M. A. **85**:900 (Sept. 19) 1925.

In a recent epidemic of thrush affecting fifteen infants, the authors used local applications of a 1 per cent. aqueous solution of gentian violet, without other treatment. The solution was applied not oftener than once a day except in one case. One patient was dismissed before the effects of treatment could be observed. Of the fourteen remaining, seven showed an apparent cure in one day or less, five in from two to three days and two in from four to five days. In three instances the lesions returned and in each instance again disappeared after one application of gentian violet. While the effects of this treatment were strikingly uniform in this series of fifteen cases, the authors, in the absence of careful controls, feel justified only in presenting these data and recommending the dye for a trial.

SCARLET FEVER: ETIOLOGY, PREVENTION AND IMMUNIZATION, AND ANTITOXIC TREATMENT. WILLIAM H. PARK, J. A. M. A. **85**:1180 (Oct. 17) 1925.

The author concludes that the antiscarlatinal serum produced by Moser and Savchenko produced the same therapeutic results as that now produced

by the Dochez method or by the subcutaneous injection of known doses of toxin. The value of the earlier products was greatly handicapped by the lack of any means such as the Schultz-Charlton and Dick methods for estimating their antitoxic potency. Because of this lack of knowledge, serum weak in antitoxin was undoubtedly frequently used, with disappointing results. The antitoxin serum should be given in sufficient amount as early in the disease as possible. When thus given, the results in most cases are strikingly favorable. The early use of antitoxin probably frequently prevents the development of complications. Antitoxin is useless after the rash has disappeared and has no effect on the later septic complications. In moderate cases it should be given intramuscularly. In severe or toxic cases it should be given intravenously. As a rule, a single dose of sufficient size is enough, but in severely ill patients, in whom the symptoms return, a second dose in from twelve to twenty-four hours is often desirable. It is too early to state whether the serum should be given in very mild cases, since the serum sickness is often more annoying than the scarlet fever. The refined antitoxic serum produces fewer and less severe rashes than the unrefined, and should in time be the only preparation used. A unit should be adopted, so that results from different dosages may be compared. The one suggested at a recent meeting of immunologists in Washington seems to be suitable. One unit is defined as the amount of antitoxin that neutralizes 100 skin test doses (Dick), as determined by an intracutaneous test in man. A dosage between 2,000 and 10,000 units will probably suffice in the great majority of cases. A few of the failures of antitoxin may be due to the fact that some toxic cases may be due to streptococci that produce other toxins than are neutralized by the antitoxin used. This is an interesting problem for future study. Whether it will be of marked advantage to combine an antimicrobial serum with the antitoxic serum is still doubtful, but merits careful investigation. Such a serum used alone in the past has given doubtful results, but combined with antitoxin it may add to the benefit produced. There would thus be a return to a serum such as was used by Moser, but with knowledge of the potency in both the bactericidal and the antitoxic properties.

BONAR, Salt Lake City.

THE POSSIBILITIES OF PHYSIOTHERAPY IN THE PREVENTION AND TREATMENT OF THE PARALYSIS FOLLOWING ANTERIOR POLIOMYELITIS. E. B. KESSLER, J. Radiol. **6**:318, 1925.

After considering the pathology of this condition the writer offers a plan of procedure. At the end of the acute stage, the disappearance of tenderness, diathermy applied over the spine is suggested as an aid in carrying away broken down inflammatory products, as well as to bring an increased supply of blood. A static condenser discharge is recommended to overcome the increased congestion resulting from the diathermy. A weekly ionizing dose of roentgen ray is recommended for its solvent effect on sclerosed tissue. Diathermy and slow sinusoidol current are of value when applied to the affected muscle groups in preventing muscular atrophy and loss of power. The quartz light is suggested as an aid in promoting general health and nutrition. Such an outline for treatment of poliomyelitis deserves attention. The author makes no direct reference to the use of splints, and one gets the impression that he does not consider them routinely necessary. This is not the generally accepted idea that rest and support of the relaxed muscles are of paramount importance in preventing deformity. Electricity is not new in the treatment of this condi-

tion but in most medical centers is at present little used. The result of a series of cases treated with diathermy and the sinusoidol current under controlled conditions is necessary before their general recommendation will be accepted.

CHAMBERLAIN, Chicago.

BALANTIDIAL DYSENTERY, WITH REPORT OF CASE. DAVID T. FORD, Northwest Med. **24**:558 (Nov.) 1925.

Ford reports a case of dysentery due to *Balantidium coli*, a constant inhabiter of the intestine of swine. The patient was a woman, aged 29, who complained of diarrhea of ten years' standing, acquired while living on a farm where swine were kept. She usually had from four to ten foul, loose stools a day, and there showed balantidia in large numbers. She was given intravenously 17 c.c. of 1 per cent. mercurochrome-220 soluble, which gave a severe reaction, but caused a perceptible diminution of the number of parasites. One month later, a course of three weekly doses of neo-arsphenamin (0.4, 0.6 and 0.6 gm.) were given, with excellent results. Colonic irrigation with 1:5,000 acriflavine solution was given in addition to the other treatment.

SCOTT, Philadelphia.

THE TREATMENT OF PNEUMONIA IN CHILDREN WITH MERCUROCHROME INTRAVENOUSLY. LEWIS D. HOPPE and W. T. FREEMAN, South. M. J. **18**:784, 1925.

The authors report favorable results with the injection of mercurochrome-220 soluble solutions both intravenously and intraperitoneally in pneumonia in infants and children.

The technic of administering the drug is as follows. A sufficient quantity of mercurochrome to make a 1 per cent. solution is dissolved in distilled water and filtered. Only freshly prepared solutions should be used. The usual dose is 6 mg. per kilogram of body weight. The authors prefer the intraperitoneal route. They found a 1 per cent. solution nonirritating to the peritoneum. The absorption is rapid, and the clinical effect on the patient seems to be as good as when given intravenously.

In children, there is little or no systemic reaction to the drug. A few hours after its administration there is occasionally a slight rise of temperature. Following this, there is, in most cases, a sudden fall. The decline may be so abrupt that it resembles a crisis. Sometimes there is a second rise in temperature following the initial fall. In these cases a second or a third injection may be given at twenty-four-hour intervals.

The most marked changes are seen in the clinical condition. The desperately ill child often shows favorable changes shortly after the injection, such as are seen only after the crisis of the pneumonia. This profound improvement is often seen even with no change in temperature and pulse rate.

No symptoms of mercurial poisoning, nephritis or other untoward effect have ever been observed.

The mortality of a control group of cases, which had not received mercurochrome, was 39 per cent. In the group of cases which had received mercurochrome injections it was only 8.5 per cent.

The authors believe that the favorable clinical results obtained are due, first, to bactericidal action of mercurochrome on any bacteria in the blood stream, and second, to inhibition of the growth of bacteria in the lungs.

SCHLUTZ, Minneapolis.

THE PFEIFFER BACILLUS, AGENT OF CEREBROSPINAL MENINGITIS. EUGENE URECH and WALTER SCHNYDER, Ann. de l'Inst. Pasteur **39**:769 (Sept.) 1925.

This organism has been isolated from the cerebrospinal fluid of many patients with meningitis. Most of the patients died, particularly those under 2 years of age. Bilateral deafness is mentioned as a frequent sequel.

A study was made of these organisms obtained from the upper respiratory tract and from the cerebrospinal fluid, in an attempt to differentiate pathogenic types from others. Animals were inoculated, and death was produced. The organism was isolated in pure culture from the organs, blood and spinal fluid. Intravenous injection in some cases produced no results of consequence; subcutaneous, intraperitoneal or intracerebral injection resulted in meningeal involvement, associated with septicemia. The organism was recoverable in pure culture from most of the tissues. Cultures of the upper respiratory tract were always contaminated. While a bacteremia is found at times, it is not probable that the organism can proliferate in the blood stream except as an agonal event.

Agglutination reactions indicate that the organism is pleomorphic. Immune serums agglutinate homologous and related strains to a limited extent.

It was impossible to differentiate in any way the strains found in the upper respiratory tract from those producing meningitis, either morphologically or by virulence tests.

BOYD, Iowa City.

THE VIRUS OF HEINE-MEDIN DISEASE (ANTERIOR POLIOMYELITIS). ANDREA CESA, Clin. Pediat. **7**:397-404, 1925.

The author was able to isolate and culture what he believes to be the virus of anterior poliomyelitis. Cultures were made during the first week of the disease. The virus was cultivated on a Di Cristina modification of Noguchis medium. Examined by the hanging drop method the organism was seen as slightly motile. Stained specimens under ordinary microscopic magnification showed the organisms to be diplococci with marked relative polymorphism. Some were elongated and some ovoid, and others had clubbed ends. They did not grow on the ordinary culture mediums.

ZAMBARANO, Northville, Mich.

THE DIPHTHERIA ANATOXIN INTRADERMAL REACTION. A. REDLICH and F. RONCHI, Pediatria **33**:813, 1925.

Redlich and Ronchi, following the method described by Zoeller, have tried the intradermal anatoxin test in a large series of cases. They used two-tenths of 1 c.c. of a 1 per cent. solution of antitoxin for the test, and also did the Schick and control tests in the same series of cases. They believe that a positive anatoxin test means that the body is sensitive to the protein of the diphtheria bacillus. When positive, there develops at the site of the injection, a circumscribed, infiltrated, reddened area which is at its height the second and third days after the injection, and then gradually disappears. The authors tested thirty children with diphtheria, thirty with measles, nineteen with scarlet fever, twenty-four with other diseases and fifty new-born infants and their mothers. The anatoxin reaction seemed to be independent of the Schick reaction, being positive in some patients with a negative Schick reaction, and vice versa. In children ill of diphtheria, the reaction was frequently negative during the first few days of the illness; later in the course of the disease, the

reaction was more frequently positive. During the eruptive stage of the exanthem, the reaction was rarely positive but tended to become positive during convalescence. In the new-born infants the reaction was negative.

The importance of the test, the authors say, is that it stresses the significance of diphtheria allergy from the standpoint of the organism's defensive powers. In sixty-six children who received toxin-antitoxin, six months later, sixty showed a negative Schick while twenty-four showed a positive anatoxin reaction. The authors believe that persons who give a negative Schick and a positive anatoxin reaction are naturally immune, but are allergic to the protein of the diphtheria bacillus, whereas those who give a negative Schick and anatoxin reaction, are both immune and nonallergic.

DE SANCTIS, New York.

METABOLISM IN SCARLET FEVER. J. PETHEO, Orvosi hetil. **69**, 1925.

Ammonia of the blood and urine gives from three to four times higher values than normal. Total nitrogen is high, nonprotein nitrogen is always high in severe cases. Urea is normal, amino-acids are higher. Uric acid gives values from four to five times higher than normal. Blood sugar is first low and increases later. Ketone in the blood bodies, even in cases with no acetone in the urine, show from three to ten times higher values than normally.

ZENTAY, St. Louis.

PROPHYLAXIS OF MEASLES. O. SRAMEK, Cas. lék cesk. **63**:1601 (Nov. 1) 1924.

The author reviews measles prophylaxis since the work of Home (1718-1813). Sramek used convalescent serum and was able to prevent, abort or minimize measles in contact cases. He feels that the serum is most active early in convalescence. A dose of 3 cm. in patients up to 4 years of age on the first day, from 5 to 6 cm. on the second day or 9 cm. on the third day of diagnosis of the contact case gave protection. The contagiousness of the mild form and its effect on activating old tuberculosis is brought out. More lasting immunity is produced by passing through a mild form than by preventing the disease. Syphilis and tuberculosis must be ruled out before using convalescent serum, but since tuberculin tests are negative in measles a most careful examination and history of the donor must be obtained.

STULIK, Chicago.

Chronic Infections

TREATMENT WITH INTRAPERITONEAL INJECTION OF NEO-ARSPHENAMIN. HEYWORTH N. SANFORD, J. A. M. A. **85**:242 (July 25) 1925.

The author concludes from the results of experiments on animals and the clinical data obtained from ten cases, that neo-arsphenamin can be given intraperitoneally to infants with safety. While the absorption of neo-arsphenamin is not as rapid by this method as with the intravenous injections, the drug is absorbed with sufficient rapidity to act in any condition. This method is thought to be ideal for use in children, in whom the small veins make the injection difficult and in whom active treatment is imperative.

TONIC NECK REFLEXES IN TUBERCULOUS MENINGITIS IN CHILDREN. I. S. WECHSLER, J. A. M. A. **85**:510 (Aug. 15) 1925.

The author has observed tonic neck reflexes in a little less than half the number of cases of tuberculous meningitis studied. These occurred with greatest

frequency in children under 3 years of age. To obtain the reflexes, the child is placed flat on the back and the position of the limbs is observed. The head should be rotated to one side so the chin points to one shoulder. The head should be held in this fixed position. After a few movements, one should note the position of the limbs, observing which flex and which extend. The process should then be reversed. When the reflex is positive, after a short latent period of a few seconds, one or both limbs on the side to which the chin is turned become extended, show a tendency to extension or at least become hypertonic while those on the other side tend to flex and become less rigid. Sometimes as a part of the flexion reflex, a spontaneous Babinski sign may be observed on the occiput side. The sign is physiologic and anatomic and is not of especial pathologic significance. Any lesion at the middle brain level may, on occasion, give rise to the reflexes. That it was found in a number of cases of tuberculous meningitis is merely clinical proof of what is known of its pathology, namely, that it is frequently or preponderatingly a basilar meningitis. The sign has not been elicited in other forms of meningitis. It rarely occurs in few other clinical entities in children.

BONAR, Salt Lake City.

MEDIASTINAL AND LUNG TUBERCULOSIS. ROLAND G. BREUER, J. Radiol. **6**:307, 1925.

In over 90 per cent. of the last thousand cases coming under the author's observation, a history either of positive diagnosis or of presumptive evidence of tuberculosis of the mother was present. Because of her close contact, such a condition is of the greatest significance. Infection in the great majority of cases comes from inhalation or ingestion, or both, of the tubercle bacillus. Mothers' milk is not only not infective but has some tuberculosis resisting properties. The primary infection in pulmonary tuberculosis is in the mediastinal lymph glands. Because of this location physical findings are insignificant, D'Espine's sign being the one valuable finding. Not until spread of the infection with the accompanying fibrosis, attempting to overcome the advance, are other physical findings present. Demonstrable physical findings at the apex indicate a period of from five to fifteen years of actual activity, and the tuberculous process is no longer incipient. The roentgenogram is second in importance only to a complete family history, it should take precedence over physical findings.

The author routinely takes chest plates of the entire family, so far as possible, and reports a striking uniformity in the fibrosis pattern in such a family series.

CHAMBERLAIN, Chicago.

SERODIAGNOSTIC AND DIAGNOSIS OF ACTIVITY IN TUBERCULOSIS. F. KLEMPERE and A. SALOMON, Med. Klin. **21**:121, 1925.

The complement fixation reactions with the antigens of Wassermann and Besredka have been studied by the authors in a great number of cases with manifest tuberculosis and with only a suspicion of tuberculous infection. Their results are summarized:

1. The reactions of Wassermann are positive in only 73 per cent. of cases with active tuberculosis, while the Besredka antigen gives positive reactions in 89.5 per cent. of the cases.

2. In cases of certainly not active tuberculosis they give positive results in 27 per cent. and 46.7 per cent. of the cases, respectively.

3. Hence, they have no decisive value in doubtful cases.

We have no reliable methods for testing the activity of tuberculous infections. The complement fixation tests do not mean any progress in this direction.

ZENTAY, St. Louis.

THE FIXATION REACTION APPLIED TO THE DIAGNOSIS OF TUBERCULOSIS IN DOMESTICATED CARNIVORA. A. URBAIN, Ann. de l'Inst. Pasteur **39**:764 (Sept.) 1925.

The literature dealing with the diagnosis of tuberculosis in domesticated animals is briefly reviewed, and its unsatisfactory status is emphasized. The complement fixation reaction was found to be far more trustworthy than the tuberculin reaction. Urbain has confirmed this work, checking his findings by necropsy. In fifty-six cases of tuberculosis in dogs and in cats, he obtained positive complement fixation in every case. Examination of serum from seventy normal dogs yielded sixty-eight negative and two positive results. The subcutaneous tuberculin test, applied to thirty-seven tuberculous dogs, was negative in 20 per cent. of the cases, and doubtful in 18.9 per cent.

He emphasizes the danger of human beings contracting the disease from infected animals. Respiratory discharges and pus from ulcers were found to contain the Koch bacillus in abundance.

BOYD, Iowa City.

CHRONIC HYDRARTHROSIS IN CONGENITAL SYPHILIS. A. ORO, Pediatria **33**:751, 1925.

In 1919, Cantonnet called attention to a symptom of congenital syphilis that is rarely mentioned, but that occurs quite frequently; that of chronic hydrarthrosis of the large joints, especially of the knee. Ora found that chronic hydrarthrosis is more common than deafness and that this symptom should be included in the Hutchinson group, suggesting that it be called Hutchinson's quadrad instead of triad. Chronic hydrarthrosis of congenital syphilis is synovitis of the large joints, usually of the knee. It is usually symmetrical, with an insidious onset, running a chronic and indolent course, independent of bone pathology and responding to antisyphilitic treatment. In fourteen cases of syphilis, the author found this symptom present in ten, whereas deafness occurred in only two of the group. Ora cites other authors who found chronic hydrarthrosis relatively common in congenital syphilis. In the ten cases studied by Ora, the knee was the joint involved, but in two, the elbow and shoulder had been previously affected. The condition was symmetrical in only four of the series, this not following the usual distribution. There was otitis media and deafness in eight of the ten subjects. In all, the joint disturbances promptly disappeared under specific treatment for syphilis. The hydrarthrosis may not develop until adult life. The insidious onset, the chronic course, the evening tenderness, and the association of other syphilitic symptoms should suggest the diagnosis.

DE SANCTIS, New York.

CONTRIBUTION TO THE PATHOGENESIS OF FRIEDREICH'S SYNDROME IN CONGENITAL LUES. J. SVEJCAR, Cas. lék. cesk. **63**:1342 (Sept. 13) 1924.

The author feels that the underlying pathology of Friedreich's syndrome in congenital syphilis is a syphilitic meningitis with localized endarteritis in the cortical and tract areas. The differential point is that in congenital syphilis

the cortical and cord changes are secondary to the encephalomyelomeningitis, while in Friedreich's syndrome these changes are primary. Active antisyphilitic treatment is of the greatest value before the secondary changes take place.

STULIK, Chicago.

Internal Diseases

INTARVIN IN DIABETES. MAX KAHN, Arch. Int. Med. **36**:44 (July) 1925.

Intarvin, as stated by the author, is the glyceryl ester of margaric acid, synthesized in edible form in his laboratory. Its chemical formula is $(C_{16} H_{33} COO)_3 CH_2$. Ch. CH_2

He states that with intolerance for starchy foods there follows a disturbance in the assimilation of fat foods, which disturbance is dangerous to the patient.

Quoting the work done by Knoop, in 1905, he shows that fatty acids in combination with aromatic radicals are oxidized in a definite manner in the animal organism. If a higher acid than acetic acid is administered, the resultant product elminated is either the hippuric acid or the phenaceturic acid, depending on whether the side chain was of an odd or an even number of carbon atoms.

In the metabolism of fats (under normal conditions; that is, in the presence of proper carbohydrate oxidation), there is a rapid breakdown of the fatty acid radical to the four-carbon, i. e., butyric acid. The butyric acid is then rapidly catabolized to carbon dioxid and water.

This process is markedly disturbed in states of deficient carbohydrate oxidation. In the latter circumstance, the fats are primarily broken down to butyric acid but under these conditions butyric acid is decomposed first to beta-oxybutyric acid, then to aceto-acetic (or diacetic) acid. The further decomposition to acetone takes place largely in the urine itself.

The author quotes Embdem for the statement that only fatty acids of an even number of carbon atoms will yield aceto-acetic acid in transfused dogs' liver. In this way, from stearic acid (C_{18}), palmitic acid (C_{16}) is formed; from this an acid with 14, 12, 10 or 8 carbon atoms is derived, then capronic (C_6) and, finally, butyric acid and oxybutyric acid are formed.

Kahn succeeded in preparing an odd carbon fatty acid that is edible, is absorbed to the extent of 90 per cent., is catabolized in the body, and does not yield the ketone substances derived from butyric acid.

He gives the method of preparation and its physical properties. He summarized the results obtained from the use of intarvin by other laboratories and clinical workers thus: 1. It is absorbed (Benedict and West). 2. It is nontoxic (Heft, Kahn and Gies). 3. It is nutritious and substitutes, so far as nourishment goes, for natural fats (Gies, Baehr, Lundin, Modern). 4. It is catabolized without the production of the acetone substances (Kahn, Hubbard, McCann, Sansum, Lundin, Modern). 5. In the phloridzinized dog it was transformed to glucose. This is not the case in diabetic subjects. Benedict and West did not find it changed to glucose in phloridzinized dogs. 6. What the end-products of the catabolism of intarvin are is a mooted point.

Dr. Sansum of the Potter Metabolic Clinic, California, is quoted as follows:

1. Intarvin, unlike natural fat, may be used in the diet of the patient with severe diabetes without fear of acidosis. 2. The substitution of natural fat for intarvin in the amounts used in the experiment promptly brought on an alarming acidosis. 3. The foregoing severe acidosis was promptly relieved when the intarvin was restored to the diet.

The results obtained in patients are summarized by the author: 1. It nourishes them, so they gain weight. 2. It allays their sense of hunger. 3. It strengthens them, so that they do not feel so "weak and tired," the usual complaint of the diabetic patient.

LOEBER, New Orleans.

THE SEASON OF 1924 ON THE BOSTON FLOATING HOSPITAL: CASE REPORTS BY MEMBERS OF THE STAFF. LAWRENCE W. SMITH, Boston M. & S. J. **193**:101 (July 16) 1925.

The differential diagnosis in each of these cases is ably and interestingly discussed in the original article.

CASE 1.—A female infant, aged 2 months, referred to the hospital with a diagnosis of bronchopneumonia, died one and one-half hours after admission, before satisfactory examination could be made. Necropsy disclosed that all pathologic changes were restricted to the heart and lungs. The heart was fully twice its normal size and presented a complete transposition, with the apex appearing in the seventh interspace on the right side, 2 cm. outside the anterior axillary line. The transverse diameter of the heart was 8 cm. Careful dissection following fixation presented evidence of all four of the common congenital defects, including a completely patent interauricular foramen, a partially patent interventricular septum, an almost complete stenosis of the pulmonic valve, a widely dilated ductus arteriosus and atelectasis of the posterior margin of the lower lobe and practically complete atelectasis of the middle lobe of the right lung. There was also partial atelectasis of the apex of the upper lobe on the right side, due apparently to the cardiac hypertrophy and displacement. On the left side there was one small area of partial atelectasis in the left inferior posterior border of the lower lobe.

CASE 2.—A girl, aged 15 months, was being treated for tuberculosis of skin. A swelling about the size of a walnut was seen in the middle of the left tibia anteriorly. It was not reddened nor hot; the skin was normal, and the mass fluctuant, slightly tender, quite freely movable and apparently not definitely attached to the bone. Laboratory reports showed: hemoglobin, 70 per cent.; white blood cells, 18,000; lymphocytes, 65 per cent.; mononuclears, 9 per cent.; polymorphonuclears, 26 per cent.; red blood cells, normal; Wassermann reaction, negative; sputum, negative. Roentgen-ray examination of the chest suggested tuberculosis, of the tibia, chronic osteomyelitis, also unsuspected lesions of the left radius and right humerus. The tuberculin reaction was strongly positive. The tibial mass was aspirated and 3 c.c. of blood tinged fluid with coarse flecks of fibrin obtained, and animal injection confirmed the diagnosis of tuberculosis of bovine type. Two weeks after admission the child developed acute conjunctivitis, iritis and secondary glaucoma in the right eye. Examination seven months later showed definite improvement in the general condition, and bone lesions under heliotherapy and general hygienic measures.

CASE 3.—A girl, aged 15 months, developed, 4 days before admission, an acute diarrhea of about eight green, watery, foul stools a day. She lost her appetite and started vomiting everything she ate. A positive diagnosis was never made, but the possibilities of the following differential diagnosis were suggested: gastric or duodenal ulceration with hemorrhage, typhoid fever with intestinal ulceration, Henoch's or hemorrhagic purpura, Meckel's diverticulum, or simply hemorrhage associated with some upper respiratory tract infection. The patient was transferred to another hospital on the closing of the boat.

CASE 4.—A girl, aged 21 months, presented a case of difficult chronic intestinal indigestion, interesting because of some symptoms and the diagnosis made of Henoch's purpura while in Boston City Hospital three months before this illness.

CASE 5.—A girl, aged 10 months, presented a case of bilateral tuberculous dactylitis of the thumbs with a small discharging sinus lined with hyperplastic granulation tissue in the cleft between the thumb and index finger on each hand. She was treated with heliotherapy and ultraviolet therapy.

CASE 6.—A boy, aged 3 months, was taken suddenly ill, twenty-four hours before admission, with a convulsion, which was followed by twenty additional ones during the first twenty-four hours and thirty convulsions during the next twenty-four hours after admission. Although the family history was negative and the mother denied the possibility of syphilitic infection, her spinal fluid and blood Wassermann reactions were found positive. Intensive antisyphilitic treatment was given the baby with good results, and the spinal fluid Wassermann reaction was positive. Later the blood also became positive and the eruption became definitely syphilitic in appearance. The author says, "It is the youngest case of syphilitic meningitis which we have been able to find in a casual search of the literature."

CASE 7.—A boy, aged 6 months, was admitted with the diagnosis of infectious diarrhea. The illness which had lasted for four days started with pain, restlessness and insomnia, and then several stools containing blood and mucus. There was occasional vomiting from the onset. He was improved the next day. The temperature on admission was 103.5 F. The abdomen was distended; rectal examination revealed no mass; there was some fecal matter and blood; all symptoms were relieved by enema. The next day there was a sudden change in condition with marked prostration, a temperature of 105 F., persistent vomiting, and abdominal distension temporarily relieved by gastric lavage. An emergency operation was performed, showing intussusception from the ileocecal valve to the splenic flexure, and the intestines gangrenous. The baby died as the operation was completed.

CASE 8.—A boy, aged 12 months, breast fed since birth had a skin eruption about the inguinal region at 3 months, and later persistent stomatitis diagnosed as thrush, which interfered with nursing and nutrition. He weighed 4,890 gm., and had six teeth. There was a papular seborrheic eruption on the scalp and the temples and in the genital region, and marked gingivitis and stomatitis; the liver and spleen were enlarged; there was a small ischiorectal abscess. The Wassermann and intracutaneous tuberculin reactions were negative; the blood picture showed: 5,200,000 red blood cells; 60 per cent. hemoglobin; white count not mentioned; differential count normal. Cultures of the mouth and skin lesions yielded a Monilia apparently between the albicans of thrush and psilosis of sprue. The patient improved for a time but finally succumbed. Necropsy revealed granulomatous lesions in the liver, lungs, kidneys and gastro-intestinal tract; also hydrothorax and atelectasis of lung on the right side.

CASE 9.—A girl, aged 19 months, was brought to the hospital because of severe anemia, failure to gain in weight and marked weakness. The temperature was 102 F.; there was some jaundice. She showed some signs of rickets. The principal symptom was an enlarged abdomen with the liver 5.5 cm. below the costal margin and an enormously enlarged spleen which reached the symphysis pubis. The Wassermann and Pirquet reactions were negative. The blood showed an increase in bilirubin, 1,952,000 red blood cells, 23,000 white

blood cells, 30 per cent. hemoglobin, 300,000 platelets, 39.6 per cent. polymorphonuclears, 12 per cent. small lymphocytes, 30.4 per cent. large lymphocytes, 17.4 per cent. large mononuclears, and 0.6 per cent eosinophils; extreme poikilocytosis, anisocytosis, punctate basophilia, achromia and polychromatophylia; many cells showing Cabot's ring bodies, and Howell-Jones bodies; also megaloblasts and normoblasts; the reticulated red cell count was 5 per cent., and the color index 1.2. The fragility test began at 0.56 per cent. and was complete at 0.42 per cent. The patient had four blood transfusions, and the red cells increased to 4,800,000 and hemoglobin to 65 per cent.; but later there were 3,000,000 red blood cells, from 10,000 to 15,000 white blood cells and hemoglobin 50 per cent.; so splenectomy was performed and the red cells increased to 4,000,000 and the white cells to 60,000. The fragility test began at 0.36 and was complete at 0.18 per cent. There were as many as 20,000 nucleated red cells per cubic centimeter. Marked clinical improvement was also noticed. Later there were 2,000,000 red cells and 50 per cent. hemoglobin, and white cells up to 100,000. Blood transfusion was given and the red cells rose to 3,000,000, the white cells to 165,000 and the nucleated red cells to over 1,000,000 per cubic centimeter. During the following two months there was marked clinical improvement under heliotherapy with red cells, 3,500,000; white cells, 150,000; 75 per cent. lymphocytes, and 25 per cent. polymorphonuclears, the fragility test beginning at 0.34 and complete at 0.10 per cent. The differential diagnosis was congenital hemolytic anemia.

CASE 10.—A boy, aged 3½ months, was admitted with the diagnosis of pylorospasm. He was treated with thick cereal feeding with splendid results.

GENGENBACH, Denver.

THE GROWTH AND DEVELOPMENT OF DIABETIC CHILDREN. ELLIOTT P. JOSLIN, HOWARD F. ROOT and PRISCILLA WHITE, J. A. M. A. **85**:420 (Aug. 8) 1925.

The authors have reviewed the 302 cases of diabetes, beginning in children before the age of 15 years. They conclude that the gain in weight of the diabetic child treated with insulin resembles that of the normal child, but the diabetic child is still underweight for his age, though often not for his height. The increase in weight of the diabetic child treated with insulin, though occasionally normal, is usually below that of the normal child, either at the expense of growing thin or while being well nourished. The sexual development of the diabetic child appears assured. The prognosis of the diabetic child treated with insulin is still problematic, but clinical, therapeutic and pathologic evidence sets no bounds.

STATIC PERITONITIS IN THE MALNOURISHED INFANT. JOHN A. FOOTE, J. A. M. A. **85**:720 (Sept. 5) 1925.

Premature, toxic, and typically athreptic infants display symptoms of peritoneal injury in a manner that may be termed static. One patient showed infection through the umbilical vein. In intussusception in the athreptic infant, pain, tumor and vomiting may be seen only late in the disease and diagnosis may be difficult. Even a slight distention, not reducible by enemas, in emaciated infants should be a contraindication for intraperitoneal instillation of salt solution or of blood. A gain of weight after this procedure in desperately ill athreptic infants means a nonabsorbing peritoneum. Usually by the time it is possible to establish the diagnosis with certainty, treatment is unavailing. Hence, the need for prophylaxis of athrepsia by breast milk feeding and care

as to the hygiene of the infant in the first weeks of life. The use of pituitary extract to promote peristalsis in young infants is fraught with danger, since it readily produces intussusception.

BONAR, Salt Lake City.

TOXIC GOITERS OF THE ADOLESCENT AGE. J. EARL ELSE and BARTON PEDEN, Northwest Med. **24**:413 (Sept.) 1925.

Else and Peden classify the cases of adolescent goiter treated in the Goiter Clinic of the University of Oregon Medical School as follows:

1. Simple goiter of the colloid, diffuse hyperplastic and localized hyperplastic types.

2. Toxic goiter, of the diffuse hyperplastic and localized hyperplastic adolescent types, exophthalmic goiter and toxic adenoma.

3. Tumors, adenoma and sarcoma.

Toxic hyperplastic adolescent goiter was the most common of the toxic types. If properly treated, this requires no operation; if improperly treated a permanent goiter develops. Adenoma and exophthalmic goiter occur and require surgical procedures.

HYPOTHYROIDISM. W. A. TAYLOR, Northwest Med. **24**:422 (Sept.) 1925.

Taylor considers the following conditions sometimes due to hypothyroidism. In obesity, dietary restriction usually suffices, but thyroid will hasten the result and is safe if the basal metabolism is watched. In thin, weak, and listless patients with anorexia, minute doses of thyroid are of benefit. Thyroid is of value in young girls with severe dysmenorrhea, and is also of value in the mastoid of young unmarried women. Women at the menopausal age with swelling of the hands and feet are helped by thyroid. Colloid goiter and the goiter of puberty are usually benefited by thyroid extract, as are long standing cases of exophthalmic goiter which have become hypothyroid. He considers infantile myxedema in the congenital form, in the early form appearing during the first year, and in the mild, attenuated form which is difficult to recognize and is characterized by failure of mental and physical development. Taylor's dose of dry thyroid extract averages 0.01 gm. for every 6 months of age, minimum dose 0.001 gm., maximum dose 0.05 gm. He recommends alternation of treatment and rest periods.

NEPHRITIS. SOME NEWER VIEWPOINTS CONCERNING ITS NATURE AND TREATMENT. MCKIM MARRIOTT, Northwest Med. **24**:472 (Oct.) 1925.

Marriott describes the two commonly occurring nephritides of childhood. The first, or parenchymatous type, he believes to be caused by a staphylococcus infection, most often in the paranasal sinuses, which produces widespread systemic effects, the kidney being only one organ involved. Infection produces a substance which lowers the surface tension of the blood, causes water to be retained in the tissues and protein to pass into the urine. There is no failure of kidney function and no retention of nitrogenous metabolites. The second, of hemorrhagic glomerular type, is usually due to a streptococcus hemolyticus infection, most often in the tonsils or mastoid. Toxins produced by this infectious process are believed to cause an injury to the capillaries, evidenced by the renal hemorrhage and by changes in the capillaries of the nail bed. This causes blood pressure, eyeground changes, nitrogen retention, and

more or less severe uremic symptoms. Marriott says that renal pathologic findings will explain the phenomena of neither of these types, and that they are no more primary diseases of the kidney than syphilis and measles are primary diseases of the skin. Marriott includes a chart of differential diagnosis prepared by Clausen.

PELLAGRA: SECONDARY TO VOLUNTARY INANITION. NOBLE W. JONES, Northwest Med. **24**:559 (Nov.) 1925.

Jones reports pellagra occurring as a result of long continued voluntary starvation. Following an acute digestive upset, believed to originate in the gallbladder, the patient feared the pain following the ingestion of food and started a voluntary fast. She lost a great deal of weight and developed chronic diarrhea. After nine months of self imposed starvation, the patient was admitted to a hospital and feeding was forced. At the end of one month after improvement and some gain in weight, the skin phenomena of pellagra appeared. This improved and disappeared as the patient's systemic condition became normal.

SCOTT, Philadelphia.

SOME STUDIES ON THE INCIDENCE OF GOITER AMONG THE SCHOOL CHILDREN IN MANITOBA. T. GLEN HAMILTON, Canad. M. A. J. **15**:1017 (Oct.) 1925.

This study is based on a survey of 2,329 children in the city of Winnipeg and several country points in Manitoba.

The incidence varied in the different schools from 85.4 per cent. in one school to none in an Indian school. Analysis of 1,609 cases according to race showed that the Indians had very few cases of goiter; the Scotch, English, Irish and Germans a large number of slight cases, while Rumanians, Polish and Jews showed the largest proportion of moderate and marked goiters in the total number.

No marked difference was found between sexes in earlier school ages. With increasing age, goiter predominates in girls; after puberty there is an apparent reversion to normal which is not so marked among girls.

The authors believe that there are various factors besides the water supply causing the large incidence of goiter. No causes are given, however.

MOORE, Omaha.

REPORT OF A FATAL CASE OF PERSISTENT HYPERTROPHIED THYMUS. JUAN L. MORALES, Arch. españ. de pediat. **9**:392, 1925.

The patient, a girl, aged 11, was admitted to the clinic presenting intense difficulty with deglutition, attacks of suffocation occurring chiefly at night, marked inspiratory stridor and pronounced undernutrition. This condition had existed for about two months. There were intervals in which the child was free from symptoms.

Physical examination of the throat, esophagus and chest for foreign body, diverticula or tumor proved negative. Fluoroscopy and roentgen-ray examination of the chest showed no abnormal shadows.

The condition progressively grew worse. Intubation failed to give relief, and the patient died in asphyxia. At necropsy an enormous thymus was found, extending from the tracheal bifurcation down to the diaphragm. Its weight was 27.7 gm. There was no evidence of tracheal or esophageal compression. The entire respiratory tract appeared to be normal.

The author believes that functional alteration of the thymus was chiefly the cause of death.

Radiotherapy and possibly subcapsular thymectomy are the two chief therapeutic procedures to be considered. Intubation and possibly tracheotomy should be performed if asphyxiation is imminent. Antisyphilitic treatment should also be thought of.

A Case of Multiple Cartilaginous Exostosis. C. R. Ostergaard, Ugesk. f. Læger **37**:795, 1925.

This brief paper is a case report of a boy, aged 9 years, suffering from multiple exostosis of the long bones. The etiology of this condition is not established. Rachitis is considered in that the exostosis forms at the epiphyses and the growth of the exostosis ceases when union of the epiphysis and diaphysis takes place.

Schlutz, Minneapolis.

Nervous Diseases

Spinal Drainage. Value in the Treatment of Early Poliomyelitis. J. C. Montgomery and W. C. C. Cole, J. A. M. A. **85**:890 (Sept. 19) 1925.

The authors' studies strongly suggest a possible beneficial effect on the outcome of the disease to be derived from early and repeated subarachnoid drainage. The evidence of beneficial effect is sufficiently suggestive to necessitate the control of this factor in any studies of clinical poliomyelitis that attempt to evaluate a therapeutic procedure of which lumbar puncture is a part. This study was made on twenty-six patients with poliomyelitis, twenty of whom were seen before the complicating paralyses occurred. Of the clinical signs, aside from hyperesthesia and pharyngitis, those most constantly present were neck rigidity and resistance to anterior flexion of the spine, these signs being found in 92 per cent. of all cases. Kernig's sign was present almost as frequently, 88 per cent.

Chorea Insaniens: Report of a Case with Recovery. Orlando H. Petty and Howard W. Schaffer, J. A. M. A. **85**:973 (Sept. 26) 1925.

A case of chorea insaniens in a white girl, aged 12 years, is reported. It is of special interest to note the rapid and complete recovery in such a short period of time.

Bonar, Salt Lake City.

Stammering as a Neurosis. M. S. Gregory, J. Nerv. & Ment. Dis. **62**:371-375 (Oct.) 1925.

The author feels, while not rejecting heredity, that stammering in childhood can be explained as a result of neuroses developed by pampering and by overcaressing the child during infancy. The infant is born possessed with emotion mass and eroticism which should be overcome early. As a result of poor training, repressions take place in the child's mind and a fear or dread complex may develop as he becomes older, often at 3 to 5 years of age when speech is developing. Some secret or forbidden knowledge may be in his mind, yet he is conscious of it as he tries to talk or ask questions. Stammering results; the habit grows which he may convert into a symptom and enjoy being ill. Later in life he compensates in lines in which he can excel, since he is sensitive and feels inferior. But the neurosis persists.

As to treatment, persuasion and suggestion are recommended, and adjustments after a psychanalysis. A case report is given.

FLOYD, Iowa City.

DISTURBANCES OF HEAT REGULATION BY LESIONS OF THE CENTRAL NERVOUS SYSTEM. L. RIBADEAU-DUMAS and A. FOUET, Rev. franç. de pediat. **1**:3, 1925.

The authors report a case of an infant in whom extreme variations of temperature were noted. The temperature was practically uninfluenced by external heat or cold. The general nutrition was maintained satisfactorily. Convulsions developed and became more and more frequent, and the infant died suddenly at 10 weeks of age with a temperature of 37 C. Necropsy showed softening of the surface of the brain, degeneration, hydrocephalus, meningitis, endarteritis and periarteritis. This case is compared with one reported by Feer, in which there was severe obstetrical injury with practically complete destruction of the cervical cord and resulting paralysis. In this case the variation of temperature was not so extreme and it varied definitely with that of the environment. It is suggested that in the first case the fever was due to the resorption of products produced by the brain changes, and that the low temperatures represent organic fatigue. In the second case the inability to maintain a normal temperature may be due to an interruption of the sympathetic nerves. Neither case points to the existence of a definite thermic center, nor do the authors think that any one factor, either nervous, glandular, endocrine or humoral, can be considered of sole importance in so complex a subject as heat regulation.

CLINICAL AND EXPERIMENTAL RESEARCHES ON INFANTILE TETANY. E. LESNÉ, R. TURPIN and C. O. GUILLAUMIN, Rev. franç. de pediat. **1**:40, 1925.

In the introduction, the authors note the theories thus far advanced to explain the phenomenon of infantile tetany, namely; parathyroid deficiency, toxicity and calcium deficiency. In this study made on fifty cases, they consider first, the clinical manifestations, second, the electrical reactions, and third, the physical chemistry of the blood plasma.

Of the clinical determination of latent tetany, Chvostek's sign is of the greatest value. This, however, is not present in its classical form after the seventh month. In addition, the authors consider spasms of the muscles of the digestive tract, such as pylorospasm, and certain psychic manifestations, such as disturbed sleep, as evidences of latent tetany. Of the thirty-three cases of latent tetany, twenty-two showed clinical evidence of rickets, whereas this was present in only five out of the seventeen cases of manifest tetany.

The electrical irritability was tested according to Lapicque's conception, the chronaxia being considered as the only true measure of excitability. Whereas normally this is rather constant for a given muscle, in both latent and manifest tetany it is characterized by considerable variation. The instability is probably due to changes in the physicochemical state of the muscle.

In the study of the physical chemistry of the blood, the authors concern themselves, not with the total calcium in the blood plasma, but with the calcium ion concentration, since it is this fraction of the calcium, alone, which modifies the permeability and excitability of the cells. Since this varies directly with the hydrogen ion concentration divided by the bicarbonate ion [HCO_3] concentration, according to the formula of Rona, these determinations were also made. In the cases of latent tetany there was a lowering of the calcium ions with an increasing p_H, while the alkali reserve remained within normal limits. This

was also true in manifest tetany, except that in three cases there was a definite increase in the alkali reserve. All effective therapeutic agents are shown to act in restoring the normal acid-base equilibrium, and thereby increasing the calcium ion concentration. This conception of the shortage of calcium ions, brought about by a shift of the acid base relationship in the direction of a hyperalkalinity, reconciles the two theories of hyperalkalinity and calcium deficiency, which have heretofore been advanced as explanations of the phenomenon of tetany.

LESLIE, Chicago.

DEFECATION OF CHILDREN AND ITS RELATIONSHIP TO ENURESIS. E. STIER, Ztschr. f. Kinderh. **30**:125 (March) 1925.

In contrast to the copious literature on enuresis, defecation has received little attention in the pediatric as well as in the neurologic and psychiatric literature. Of 1,000 cases that have come under Stier's observation as psychiatrist and neurologist for the schools from 1920 to 1922, soiling was the chief or secondary symptom in twenty-eight school children, nineteen boys and nine girls. This does not include idiots or imbeciles. Some children learn to control their bowels relatively late because of an overirritability of the peripheral nervous system or because of insufficient development of the central or psychic inhibitions. Similar conditions prevail in enuresis, but in soiling, both types of disturbances are more marked. Any intestinal disturbance which causes a pathologic irritability of the rectum aggravates involuntary defecation. Decreased inhibition leads to habitual soiling only if either the nervous tonus of the anus is too low, when there is marked mental deficiency or when the feeling of repugnance to soiled clothing is absent or not strong enough to produce sufficiently strong impulses to defecate without soiling. In the first group three cases are reported in which there was a combination of increased irritability and a constitutional decrease of inhibitions. These two factors alone are not sufficient. Only when temporary excitement such as fear or violent laughter occur, soiling takes place. As in all spheres of nervous overexcitability, the control of defecation increases with advancing age. All three boys were neuropathic and had normally developed or even increased feeling of repugnance to soiling. In the second group four cases are reported which were characterized by the fact that there was no overexcitability or tonus weakness of the intestines, no neuropathic constitution. The children were physically well and strong. There was decreased irritability to all sensory stimuli. They did not suffer heat or cold, had good appetite, and were indifferent to the choice of food. There were no vasomotor disturbances and no disturbance of sleep. In these children all egoistic and sexual tendencies were strongly developed, while the finer emotions were underdeveloped or lacking. This type of child shows no love for its parents, thinks only of himself, is cruel to animals, lies, steals and has no interest normal for his age. While the environment has probably some influence, the anomaly is primarily of constitutional character; a careful history reveals similar traits in relatives. This type of child forms the bulk of children of school age who soil themselves. The cause lies in an abnormal psychic constitution. They are dull and indifferent to the physical stimulus of their excretions, to the odor and discomfort of soiling, to the punishment of parents and teachers. In the majority of cases there is a perverse pleasure in the excreta. Since the disturbances of character underlying the soiling and the associated psychic anomalies are of vital importance to the communal and social life, the recognition and attention to this type of disturbance is especially indicated.

MEMORY IN BLIND AND SEEING SCHOOL CHILDREN. E. BECHTOLD, Ztschr. f. Kinderh. **30**:161, 1925.

Bechtold made memory tests on fifty blind and fifty seeing school children, and found that blind children are not necessarily superior in memory to seeing children, contrary to the frequent reports in nonmedical literature. Blindness in itself, even if congenital, does not involve a special gift for remembering. Such cases, just as in seeing children, are isolated. An important factor is the blind child's greater practice in remembering. He must exercise this faculty in order to survive the struggle for existence. Furthermore, the concentration favored by the blindness furthers hearing. This furthers the reproduction of the words heard. Besides, the blind child has a greater interest in all sounds. These factors explain why the blind children excelled the seeing children in the memory tests of senseless words. It would be expected that they were also superior in the memory tests of words with meaning. This was not so. When the word content played a rôle, the seeing children excelled over the blind. The tests showed, however, that blind children in their total faculties are able to compete favorably with those who see. The author has come to this conclusion in the course of his experience in educating and training the blind. But in public life, the blind do not receive the confidence that they deserve.

FUDAMENTALS OF PSYCHANALYSIS. P. SCHILDER, Ztschr. f. Kinderh. **30**:203 (June) 1925.

In the present state of knowledge of psychanalysis, an occurrence or a desire becomes a "conversion" (verdräugung) when it is painful or annoying to the individual. These occurrences are most frequently of sexual nature. The effect of the conversion may be various. The occurrence may be simply forgotten. The amnesia of the hysterical is an example of this type of conversion. But it is well known that the occurrence is not permanently or completely forgotten. It recurs in dreams, in slips of the tongue, in all conditions when attention slackens or when the person allows his thoughts to wander. In this knowledge lies the fundament of analytic technic. Another effect of conversion is the projection of occurrences from one person to another person. The reverse process may also occur. Impulses which originally had been directed against other persons may be directed toward his own person, especially if they are contrary to his moral sense. Conversion may begin in early youth. There is a constant struggle between the converted impulse or occurrence and the converting forces. Conversion may be complete or incomplete. The converted impulse has a tendency to recur. The content may be changed and a symbol take its place. The penis is symbolized by sticks, knives, clubs, snakes. The female genital organs are symbolized by rooms, boxes, pockets, pianos, bottles. An object may be symbolized by a contrast, water — urine — by fire.

Psychanalysis assumes two groups of impulses, one serving the preservation of self, the other the preservation of the race, the sex impulses. Sexual impulses, not necessarily bound to the genital, begin in earliest life. In late fetal life and in the new-born, eroticism is limited to primitive self love. The third to the fifth year, in which masturbation is regularly observed, is the time when the child is most interested in sex. The principal mechanism of hysteria lies in conversion. By means of psychanalysis the patient must learn to free himself from logical thinking and to report what is on his mind regardless of its importance and its moral value. Transference is the most important prerequisite for cure. The ideas or impulses have become free and can be trans-

ferred to other individuals. There are far reaching similarities in the thinking of the primitive, the neurotic, the child, the schizophrenic. Schilder believes that with the aid of psychanalysis it should be possible to clarify organic formation and development.

HEUMANN, Chicago.

SEVERAL CASES OF INFANTILE AND JUVENILE PROGRESSIVE PARALYSES. J. NEVERIL, Cas. lék. cesk. **63**:1551 (Oct. 25) 1924.

A combination of etiologic factors, such as alcoholic parents, trauma of the skull, strong congenital psychopathic tendency, and improper environmental development, is considered. Alzheimer regards congenital syphilis as the etiologic, or at least the predisposing, factor. Several of the children were apparently normal until 5 years, and then rapidly developed symptoms. Criminal tendency and sex precociousness and hallucinations are rare. According to the statistics cited, 13.3 per cent. of children with congenital syphilis develop progressive paralysis. A marked tendency to endocrine disturbances is noted.

STULIK, Chicago.

Diseases of the Eye

INFLAMMATION OF THE CORNEA CAUSED BY SOLUTION OF SILVER NITRATE. JULIUS FEJER, Am. J. Ophthal. **8**:862, 1925.

The author reports a case in which the midwife instilled a few drops of 10 per cent. silver nitrate solution into each eye of a new-born infant by mistake. When seen twenty-four hours later, the lids were swollen, with the corneas cloudy and rough. There was no ciliary injection. Despite very active treatment, corneal opacities occurred in the deeper layers dense enough to prohibit examination of the fundus details in one eye three months later. Many others have reported the same results under similar circumstances.

To prevent such accidents, the author suggests the use of a 1 per cent. solution of silver acetate. It is as efficient a prophylactic, causes less catarrh, does not concentrate on standing and at room temperature is only soluble in 1 per cent. strength.

WESCOTT, Chicago.

THE QUESTION OF THE ORIGIN OF SCROFULOUS CONJUNCTIVITIS. A. LOWENSTEIN, Med. Klin. **21**:845, 1925.

The basis of the origin of scrofulous conjunctivitis is to be found in allergic reactions probably of tuberculous nature. But the sensitization itself does not produce any scrofulous manifestations; for this another factor is necessary. The author thinks he will find this factor in a continued lack of vitamins in the diet. His theory is supported by the clinical similarity of severe scrofulous keratitis with keratomalacia of atrophic infants and by the good therapeutic results of a diet rich in vitamins without any other specific treatment. Scrofulous conjunctivitis is much more frequent in the early spring months than the rest of the year, probably because of the absence of vitamins in the food at that time of the year.

The supplying of vitamins is one of the main problems in dealing with scrofulous conjunctivitis. Of course, other hygienic factors should not be neglected.

ZENTAY, St. Louis.

Diseases of the Ear, Nose and Throat

PARANASAL SINUS DISEASE IN CHILDREN. L. W. DEAN, J. A. M. A. **85**:317 (Aug. 1) 1925.

The author says that 80 per cent. of his chronic cases of nasal sinus disease in infants and young children have been cured by the removal of tonsils and adenoids without any other treatment. These favorable results are due in great part to, first, the age of the patient, excluding long chronicity and, secondly, the comparative infrequency of nasal obstructive lesions in this class of cases. While nasal obstructive lesions in infancy and early childhood are not common, they sometimes are present and are improtant etiologic factors in the production of the sinus disease. In such instances, this condition must be corrected if the work can be done without interfering with the development of the nose. The local treatment of chronic suppuration of the paranasal sinuses in this class of cases consists of nasal irrigation, suction treatments and the use of protargin mild or some similar drug. An alkaline solution as hot as can be comfortably borne should be used. This form of treatment should be continued only for a few days. In chronic maxillary sinusitis, it is only sometimes advisable to aspirate the maxillary sinuses and to inject 1 per cent. protargin mild or some similar drug. This is done by passing a very small trocar through the meatal wall into the sinus. The sinus is easily aspirated, and the protargin mild is injected. Rarely is it necessary to make some opening into the antromeatal wall through which the sinus can daily be irrigated. Only very rarely is it necessary to operate on the ethmoidal and sphenoidal sinuses. They should be operated on only when the sinusitis refuses to yield to persistent energetic treatment and there is a severe local or systemic complication that would justify operating. With proper diet, especially one rich in fats; with the removal of causative factors in the upper respiratory tract, first of which is infected lymphoid tissue in the nasopharynx and the oropharynx with simple nasal treatment and perhaps antrum puncture, an apparent cure of almost all cases of paranasal sinus suppuration in infants and young children can be secured.

BONAR, Salt Lake City.

Diseases of the Skin

LIVEDO RETICULARIS. CHARLES M. WILLIAMS and HERMAN GOODMAN, J. A. M. A. **85**:955 (Sept. 26) 1925.

There is a congenital anomaly of the blood vessels which in some cases is revealed as a transitory, violaceous mottling on exposure to cold. It is so common an occurrence that no attention is paid to it as a rule, and yet the phenomenon is not universal. The cause of the condition is not yet known, principally because the condition is so transitory and unimportant that very few have given it any study. The terms, cutis marmorata and livedo, which have been applied to this condition are not to be found among the diseases of most of our textbooks on dermatology. The same or similar anomaly may show itself as a permanent mottling extremely variable both in extent and in severity. This condition may be revealed only when the circulation is impeded by some other agency. This anomaly may govern the distributions of eruptions due to other causes, notably, tuberculosis and syphilis, especially when these diseases involve the small blood vessels. Two cases of this condition are reported, and a classification is offered as a basis for future study. These two cases are considered instances of livedo reticularis idiopathica.

BONAR, Salt Lake City.

Surgery and Orthopedics

ACUTE INTESTINAL OBSTRUCTION. III. SIMPLE OBSTRUCTION. W. C. FOSTER and R. W. HAUSLER, Arch. Int. Med. **36**:31, 1925.

In experimental obstruction produced under local anesthesia, according to the authors, the postoperative animals are in practically the same condition as the human patients seen clinically. Two types of acute intestinal occlusion are thus produced: (1) acute strangulation or the surgical procedure under anesthesia; (2) acute simple obstruction.

Acute strangulation has been dealt with in a previous paper. The present paper endeavors to show that death in simple intestinal obstruction is not due to a toxemia, but to starvation.

The method and operative technic are the same as described in preceding papers. A review of the literature shows five main theories as to the cause of death in acute intestinal obstruction: (1) bacteremia, (2) perverted secretions, (3) shock, (4) toxemia and (5) dehydration. The first three of these theories have been disproved by other workers in the field: 1. Bacteremia was definitely disproved by it being shown that at death the heart's blood, peritoneum and organs are practically always sterile. 2. Perverted secretions was disproved by the draining of open isolated duodenal and jejunal loops into the peritoneal cavity. The dogs lived indefinitely and showed no toxic symptoms. 3. Shock is an acute affair always manifesting its symptoms within the first twenty-four hours. These dogs with simple obstruction live three or four weeks. Until the present the last two theories have never been definitely proved or disproved.

The authors concluded from their experiments with subcutaneous injections that vomitus is relatively nontoxic—no fatalities. They submit the following reasons for concluding that death from toxemia is improbable: (1) the relatively slight toxicity of even large quantities of vomitus; (2) the decreased absorption from the proximal segment; (3) the fact that dogs with closed, isolated loops full of extremely toxic fluids live months without showing marked toxic manifestations; (4) the quicker death in high obstruction (in this the function of the intestine is mainly secretory), and the slower death in low obstruction, in which normally much absorption occurs, and in which the intestinal secretions become more toxic because of delayed vomiting and more prolonged bacterial action; (5) the fact that furthermore, the entire clinical picture, namely, the temperature, pulse, respiratory and blood pressure variations and the general appearance of the patients and the experimental animals, is certainly not that of a toxemia; (6) the fact that in uncomplicated cases of experimentally produced intestinal occlusion, the subjects lived three or four weeks without food or water or any treatment whatever, proving definitely that toxemia is not the cause of death.

They offer starvation and dehydration as the only remaining possibility. A review of the tables outlining the experiments on the two starvation dogs shows that changes are exactly similar to those reported for normal starvation animals.

The conclusions reached by the authors are: 1. Death in uncomplicated cases of acute intestinal obstruction is due to starvation. 2. The blood chemistry changes noted in uncomplicated simple intestinal obstruction are almost identical with those found in complete starvation. Hypochloremia is not present. 3. Dehydration, in uncomplicated cases of simple intestinal obstruction, is usually found very pronounced.

LOEBER, New Orleans.

CONGENITAL ELEVATION OF THE SCAPULA WITH KLIPPEL-FEIL SYNDROME. B. NIEDERLE, Cas. lék. cesk. **63**:1689, 1743, 1784 (Nov.-Dec.) 1924.

The author describes four cases in detail. He gives a long discussion of the history, etiology, anatomy, pathology, atavism, differential diagnosis, mechanics, embryology, associated pathology, disturbance in intra-uterine pressure, exostoses on scapulae, muscle anomalies and contractures and treatment. The Klippel-Feil syndrome is the associated atrophy of cervical vertebrae producing the so-called "cervical thorax." Spina bifida cervical was found in nine of the thirteen cases reported. Cervical vertebral fusion occurs in some of these. The clinical signs are saddling of the head on the shoulders, limitation of head rotation and low posterior hair line. Because of involvement of the entire vertebroscapular region, the condition may be due to neurotrophic central pathologic change.

STULIK, Chicago.

Miscellaneous

STANDARDIZATION OF THYROID PREPARATIONS. REID HUNT, Arch. Int. Med. **35**:671, 1925.

A strong plea is made for a more efficient standard for commercial thyroid preparations, as the present condition shows a marked variation in the tablets examined, varying anywhere from 0.155 to over 0.7, in a commercial product of "2 grain tablets." A similar condition obtains in reference to the tablets on the European market. The author says: "This state of confusion is very unfortunate when attempts are being made to place thyroid therapy on a rational basis, i. e., to bring the dosage into quantitative relations to the metabolism or to other factors."

He calls attention to the close parallelism between the iodin content of different preparations of thyroid and their physiologic effect, and cautions that if iodin content of thyroid is to be used as a basis for standardization, that it is necessary to be certain that glands which are to be used in medicine do not contain "inactive iodin"; i. e., inactive in the sense that some of the iodin is not present in the combination, producing the typical effects of thyroid.

The author states that muscle tissue treated with a solution of potassium iodid and dried and powdered is alleged to have been sold as thyroid; many proprietary "antifat" remedies contain thyroid, whereas others contain potassium iodid extract of bladder wrack, and other iodin compounds. It is desirable to have tests by which nonthyroid as well as thyroid iodin may be detected, and several tests are given, including the one incorporated for this purpose in the U. S. P. VIII. By the acetonitril method, it is possible to determine with a considerable degree of accuracy how much of the iodin containing compounds is present in thyroid; this can be done when only a few milligrams of material are available. A brief review of this method is included in the paper.

Dr. Hunt concludes his paper with the following summary: 1. The physiologic activity of thyroid preparations, as determined by the acetonitril test on mice and by clinical observations, was found to be closely parallel to the iodin content. 2. Little or no physiologically inactive iodin was found by these tests in the thyroids of adult animals. 3. Very small amounts of nonthyroid iodin in adulterated thyroid preparations could be detected by the acetonitril test and also by simple chemical tests. 4. Very few of the thyroid preparations on the market comply with the U. S. P. standard; they were found to vary greatly in physiologic and therapeutic activity.

LOEBER, New Orleans.

Society Transactions

NORTHWEST PEDIATRIC SOCIETY

Minneapolis, Oct. 2, 1925

ROOD TAYLOR, M.D., *in the Chair*

CHRONIC THROMBOCYTOPENIC PURPURA. Presented by DR. E. S. PLATOU.

J. R., a boy, white, aged 7 years, was admitted to St. Mary's Hospital, Dec. 26, 1924, complaining of severe epistaxis, weakness and fever. Four days previous to admission he had complained of slight soreness of the throat and had a rather profuse hemorrhage from the nose. Packs and cautery were necessary to stop the flow of blood on this and on two subsequent occasions before admission. His fever during these four days had been rather high, a fact attributed by the mother to a vaccination "take."

Past History.—The child was a full-term, normal baby, born of healthy parents and was breast fed for nine months. Four sisters are living and well and there have been no "bleeders" among the antecedents. The patient was perfectly well until at the age of 3 years an acute infection associated with transient paralysis of the right leg occurred. This was diagnosed as infantile paralysis, although no weakness or deformity resulted. Since this illness the child had never been strong. He tired easily and had occasional mild nose bleeds.

One year ago he was admitted to the hospital after an attack of epistaxis lasting intermittently for three days. At that time his hemoglobin was estimated at about 20 per cent. and transfusion was necessary. He recovered quickly, although the hemoglobin was only about 25 per cent. when he was discharged from the hospital.

Physical Examination.—At the time of admission the boy was very weak; there was a slow oozing of blood from the nose. An extreme pallor with a slight icteric tint of the skin was noticeable and there were confluent crops of petechiae over the abdomen and thighs. The lingual papillae seemed unusually prominent and the pharynx was slightly congested. A hemic murmur was heard over the apex of the heart. There was no enlargement of the liver and the spleen could neither be palpated nor made out by percussion. The lungs were clear, the extremities negative. The temperature was 104 F., pulse 150, respiration 26. Blood examination: hemoglobin 7 per cent. (?) (Dare); red blood cells 840,000; white blood cells 1,600; the Wassermann reaction was negative; coagulation time lasted for two minutes, nonretractile clot; the bleeding time lasted for seven minutes, platelets 160,000, the differential count was normal. Smear showed a severe grade of secondary anemia with some evidence of regeneration. Transfusion, nasal cautery, opiates and calcium were resorted to and the bleeding was stopped. Six days after admission, there was a generalized coarse desquamation of the skin. The Dick test was negative and the patient was kept in isolation as a probable scarlet fever infection. Bleeding recurred on the following day and transfusion was resorted to again. This was repeated four times more during the next five weeks. A total of six transfusions of from 300 to 500 c.c. each (citrated blood) were given.

The patient was discharged on February 11, feeling very well. Blood findings: hemoglobin, 36 per cent.; red blood cells, 2,550,000; platelets, 320,000. Following discharge the boy was given ultraviolet ray exposures for two weeks.

On examination a month later, the patient looked and felt very well. Hemoglobin, 57 per cent.; red blood cells, 3,200,000; white blood cells, 4,400; platelets 80,000. At this time the patient's mother was warned of the danger that hemorrhage might occur with platelets diminishing as they were.

Two weeks later the patient was brought in after having had a rather profuse hemorrhage lasting for two hours. At this time the hemoglobin was 50 per cent.; platelet count, 40,000; bleeding time twelve minutes. The boy was kept at rest and was given large doses of calcium for one week, following which a splenectomy was performed. The spleen was moderately enlarged and there were a few small perisplenic adhesions.

Pathological Report by Dr. E. T. Bell.—Microscopic sections showed patches of diffuse fibrosis in the pulp. There was no change in the follicles. Most American pathologists call this Banti's disease, although there is no fibrosis in the follicles, such as Banti described as characteristic. The term — Banti's disease — is at the present time used to include a number of different histologic pictures.

Six hours after operation the platelet count was 114,000; the following day it was 125,000 and the bleeding time was five minutes. A week later the bleeding time was two minutes.

Since leaving the hospital, two and a half months at the time of writing, the boy has been perfectly well and there has been no hemorrhage. Blood examination (Sept. 6, 1925): hemoglobin, 62 per cent.; red blood cells, 2,550,000; white blood cells, 8,600; bleeding time, two minutes; platelets, 260,000.

Comment.—In the recent medical literature, a number of similar cases have been reported in which splenectomy has been performed. Hanrahan (Arch. Surg. **10**:639, 1925) reported thirty-five cases with features that closely resembled Oster's syndrome of chronic splenic anemia. Giffen (Minnesota Med. **8**:207, 1925) and Mayo (Surg., Gynec. & Obst. **40**:584, 1925) have reported a larger series of cases in which purpura was the outstanding symptom. Similar cases have also been reported by Brill (Am. J. M. Sc. **166**:503, 1923), Kanelson (Wien. Klin. Wchnschr. **29**:1451, 1916), Sutherland (Lancet **1**:323, 1925), Lemann (New Orleans M. & S. J. **77**:282, 1925), and others.

Rosenthal (J. A. M. A. **84**:1887, 1925), in a review of the cases of Banti's Disease at Mt. Sinai Hospital over a period of fifteen years, concludes that they can be divided into two types: 1. The thrombocytopenic, in which the platelets are diminished before splenectomy and there is a hemorrhagic tendency. 2. The thrombocythemic in which the platelets are nearly normal before splenectomy but rise far above normal afterward. He believes that the results from splenectomy with the former group are brilliant, whereas in the latter, subsequent thromboses occur and there is little if any improvement. His study is an extremely interesting one and if his conclusions prove to be correct it is a valuable contribution.

The case here reported has some of the characteristics pointed out by W. J. Mayo that are found in thrombocytopenic purpura; namely:

1. A tendency to chronic purpura. 2. A deficiency of blood platets. 3. A prolonged bleeding time. 4. Nonretractility of blood clots. 5. Enlargement of the spleen.

It is apparently the type of blood dyscrasia which is benefited by splenectomy and has the additional interesting features, that first, the hemorrhagic tendency

dates back to an acute infection associated with paralysis four years ago; second, the spleen was not enlarged sufficiently to be made out clinically; third, the bleeding was largely of nasal rather than gastric origin as is most commonly the case; fourth, the crisis resulted from a combination of a vaccination "take" and a probable scarlet fever infection.

DISCUSSION

DR. MATCHAN: I would like to ask Dr. Platou a question pertaining to the convalescence in the case reported. I have a patient now who has an elevation of temperature of from 100 to 103 F. every day. There are no complications that I can discover and the splenectomy wound is clean. The red cell count rose to 3,200,000, but the white cell count is only 6,000 per cubic millimeter. I would like to know whether Dr. Platou found such a rise in temperature in his patient.

DR. PLATOU: The convalescence of my patient was uneventful until the time of discharge from the hospital, ten days postoperatively. It seems to me that the only way a rise in temperature could be accounted for is by some complication setting in.

DR. SANSBY: Dr. Platou referred to the high platelet count following splenectomy. It seems to me that Rosenthal and others in their cases found that after splenectomy there was only a temporary rise in the platelets — in some cases to normal or above normal — after which the platelets would decrease in number until they reached the same level or even lower than they were preoperatively. Yet in the presence of this low platelet count there was no recurrence of hemorrhage.

DR. PLATOU: Dr. Rosenthal shows that the platelet count rose above normal and then dropped to normal in most of the cases. In the thrombocythemic group they rose far above normal. The results after splenectomy in practically all the thrombocytopenic cases were very good.

DR. TAYLOR: It does not necessarily follow that the results after splenectomy are bad even if the platelet count is normally high before splenectomy. In cases in which the bleeding is largely from the alimentary tract, results after splenectomy are good no matter what the platelet count.

THE THYROID OF THE NEW-BORN INFANT. Presented by DR. CHESTER A. STEWART.

From a study of a series of sections of the thyroid of new-born infants, a variety of striking histologic changes were found. The series was sufficiently large to permit the detection of definite stages in the progression of these changes.

The thyroids that were apparently normal from the histologic standpoint weighed an average of 2.5 gm. The sections contained well formed follicles filled with colloid. Evidence of new follical formation by the process of budding was noted frequently. The second group of thyroid glands also had an average weight of 2.5 gm. The histologic appearance differed from that considered as normal by an almost complete absence of colloid. In addition, the follicles were much smaller in size than normal. The impression was obtained from study of the sections that the disappearance of colloid practically offset the cellular hyperplasia present, producing numerous tiny follicles, thus preventing any increase in the gross weight of the gland.

The third series of thyroid glands presented a multiplication of cells within the individual follicles, converting the single layer of follicular epithelial cells into a double layer of cells. Colloid was also absent in these sections except for its occasional presence in marginal follicles. These glands averaged about 3 gm. in weight.

In the fourth series of sections on the thyroid glands of the new-born infants, the follicles were composed of compact masses of epithelial cells. The individual follicles were somewhat larger than in the second and third groups. Colloid is completely absent in glands of this type. The average weight of the thyroid glands of this group was over 6 gm.

The fifth group had an average weight of 16 gm. In these thyroids the follicles are rather large but are not compactly filled with cells. Instead, isolated groups of cells are scattered throughout the follicle separated by definite intercellular spaces. The histologic appearance of glands of this type indicates that a disintegration occurred among the epithelial cells formerly filling the follicles. In addition, only occasional epithelial cells remain attached to the periphery of the follicles.

This material was obtained from a series of necropsies conducted under supervision of Dr. F. L. Adair for the Children's Bureau, Department of Labor, Washington, D. C.

REPORT OF A CASE OF BREATH-HOLDING. Presented by DR. STEWART.

This child had an attack of cyanosis at the age of 5 months. The physical examination was negative, aside from roentgen-ray evidence of enlargement of the thymus. The thymus was given a series of roentgen-ray treatments and was greatly reduced in size. Following this therapy, the attacks of cyanosis continued.

Further investigation as to the cause of the attacks revealed the fact that the child brought them on voluntarily when prevented from doing things it desired. This psychic feature was present in all subsequent attacks.

A diagnosis of breath-holding was made, and the case is presented for discussion as to possible relationship with the condition of status thymico-lymphaticus. The treatment planned was to attempt to overcome the attacks by instructing the parents to ignore the child completely when holding its breath.

The attacks were of such severity that the child became extremely cyanotic, and had a temporary loss of consciousness of a few seconds duration.

DISCUSSION

DR. RODDA: I recently saw a little patient with a similar history. The baby was 11 months of age. When younger, he was given five treatments for enlarged thymus. For the last three or four months, the baby has had spasms of breath-holding, typical of the attacks described in the literature as "rage cramps." The condition in this child was extremely severe. After holding his breath for a short time, he became cyanosed, rigid, the eyes were rolled upward and there appeared to be a loss of consciousness for a fraction of a minute. The attacks were rather suggestive of petit mal.

There arises the question whether, in cases of enlarged thymus at birth, there is some constitutional tendency to attacks of breath-holding later on. The thymus in this patient is now normal.

DR. HUENEKENS: I have a patient in whom the condition was diagnosed as epilepsy before coming to me. The attacks produced unconsciousness and

cyanosis. The nurse thought the baby was dying when the attacks came on, and would pick her up at night, although told not to do so.

The baby has now completely recovered from these attacks. I showed her last week to the general practitioners enrolled in the medical short course. It was over a year ago that the child had these attacks. She is normal now but slightly neurotic. She had so many attacks that the parents took turns holding her in their arms. After she returned from the hospital she had two attacks, both occurring the first day after her return. On being completely ignored, the attacks disappeared altogether.

I would suggest that your patient go to the hospital, where the parents would have no chance to see him at all.

IMMUNIZATION AGAINST SCARLET FEVER. Presented by DR. WOODARD COLBY.

The work in immunization against scarlet fever with detoxified toxin has been done in the last seven months. We have used patients in various hospitals, Phalen Park Hospital, Shriner's Hospital, and Faribault School for the Feeble-Minded, since these patients could be under observation for a longer time and could be retested when we liked.

In the first group of cases on which the Dick test was used (children from 1½ to 12 years of age) there were 304 patients, of whom 153, or 50 per cent., were positive. Of 100 nurses, thirty-two, or 32 per cent., gave positive reactions. Of 413 cases tested at Faribault, 80, or 21 per cent., were positive. That is a very low percentage of positives. The children there, of course, were older. We tested only eight or ten under 2 years of age. The remainder were over five and up to fourteen. This also shows that contact gives immunity, just as children living in the slums develop immunity to acute infections more rapidly than children in good homes.

In determining whether the Dick test was positive or negative, we have called any redness at all a positive Dick reaction. We did this because we wanted them to be absolutely negative over a period of time, so that they could be retested after a period of observation. Under 1 year of age, the test is practically always negative and if at all positive, it is very slight. Between 1 and 2 years there are a few more with a positive Dick reaction. From 3 to 12 or 14, you get very marked positive Dick tests with reactions up to the size of a silver dollar. A total of 817 children were tested.

In immunizing, we did a small series, using the Dicks' method of three injections, and then started using the toxin mixed with sodium ricinoleate or castor oil soap, using first a 1 per cent. of soap solution with the toxin. To begin with, 1,000 skin test doses were used. The Dicks in their immunization started with 110 skin test doses, doubled it in the second injection and again in the third. We used 1,000 skin test doses with a 1 per cent. soap solution.

Using 1,000 skin test doses we injected eighteen children between the ages of 2 and 14. We repeated on the fifth day and found 48 per cent. negative. Using 1,500 skin test doses we immunized thirty-one patients and retested them on the seventh day; 66.6 per cent. were negative. Using 2,000 skin test doses we immunized forty-four children. On the eighth day we retested and found 68.5 per cent. negative. Eighteen children were given 3,000 skin test doses and 87 per cent. of these patients gave a negative reaction when retested on the eighth day. Using 4,000 skin test doses we immunized twenty-one patients; 90 per cent. were negative on the eighth day. I retested all of these 132 cases at the end of three weeks and 96 per cent. were negative. At that

time I took sixteen nurses and gave them 2,000 skin test doses. On the seventeenth day, only 37.5 per cent. gave a negative reaction, that is to say, the dose was too low.

Using seventy-seven of the patients who had positive reactions at Faribault, I gave them 3,000 skin test doses. At the end of one month 72 per cent. gave a negative reaction. That, again, is too low a dosage. Many of these children were up to 14 and 16 years of age, and the amount of toxin used was not enough for children of that age and size.

Now, to compare the results procured by Nesbitt, working with the Dick toxin and under the supervision of the Dicks, he reported a large series of cases retested at the end of three weeks with a 65 per cent. immunity. With this method, using 2,000 skin test doses and retesting on the eighth day, we have a 68.5 per cent. immunity and at the end of three weeks a 96 per cent. immunity. So with one injection we get better results than they did with the three injections made.

Using the one injection method, using untreated toxin, we had some very severe local reactions, that is, without the toxin being neutralized. We had two children with quite severe general reactions, one child, especially, who was given 175 skin doses. The patient was 7 years of age. She had an elevation of temperature and was delirious for one night.

Using the soap solution with the toxin at Faribault, there were no general reactions at all in seventy-seven cases. Dr. McBroom said there might have been a general reaction in one case, but he was not sure because the patient was a girl who complained of everything; so he reported no general reactions in seventy-seven cases.

The local reaction varies. The redness is very frequently the size of a dollar; often it is larger than that, covering quite an area with some induration. With the application of local heat, this usually passes off in from thirty-six to forty-eight hours, the lighter ones sooner. It does not seem to be very deep, but of a more superficial type. The pain does not seem very severe and the children do not complain a great deal.

The solution, of course, must be clear. If the solution is cloudy, you will get general reactions. With the first group I did, using toxin from the New York Board of Health, the solution was cloudy and I did have some general reactions. However, if the solution is clear, the results are good.

As to the keeping qualities of the toxin when mixed with the soap solution, last week I got a general reaction in a boy of 4½, when the toxin had been mixed June 12, practically three and a half months previous to the time of injection. I gave him 4,000 skin test doses and got a slight general reaction, but it lasted only a short time. So the keeping qualities of the toxin when mixed with the soap are very good.

Now as to the length of immunization, I have just retested seventy-eight patients who were immunized at the end of March. Of the seventy-eight there were fifty-five negative and twenty-three positive. That is to say, a bit over 70 per cent. were negative. That is a fairly good result, especially when we consider that these are the patients which we immunized first, that is, those which gave 70 per cent. negative Dick reactions after six months were those on whom I used 1,000, 1,500, 2,000 and a few 3,000 skin test doses (only one case in this group receiving 4,000 skin test doses). The determination that 70 per cent. of the cases were still negative was made, considering any redness at all as a positive Dick reaction. The small spot that is seen following the entrance of the needle, when there is a pin-point redness, has not

been called a positive Dick reaction, but any redness beyond that has been called a positive Dick reaction.

There is only a small series I know of reported by the Dicks in which they report that their Dick test was still negative at the end of one and a half years. I do not know how many patients that covers. But of the seventy-eight patients I immunized last March, 70 per cent. were negative at the end of six months.

DISCUSSION

DR. HUENEKENS: I have not much to add to what Dr. Colby said. I will say that before using the soap solution with this toxin, in using smaller doses, I got quite a few severe reactions. In three patients there was a typical scarlet fever rash. Since using the very much larger doses with the soap solution, however, we have had no reaction of that kind whatever. From 6 to 7,000 skin test doses gave a fairly light fever reaction.

The scarlet fever toxin, if used shortly after preparation, deteriorates fairly rapidly, in perhaps two or three months. If soap is added to it early, then it seems to retain its potency, as we have tested out cases using the same toxin at different ages.

We have had one patient in whom we gave the New York Health Department scarlet fever toxin, a very small dosage of from 125 to 250 skin test doses. This was given to a child, about 1 year old, who did not return to be retested afterward, although requested to do so. About one month ago, the child came down with typical scarlet fever, of a very mild variety, however, without any elevation temperature. At about the end of a week he developed large glands at the angle of the jaw and had a slight fever. Otherwise, the course of recovery was uneventful. I believe the child had received a slight immunity.

A series of experiments now under way show that 4,000 skin test doses do not produce permanent immunity. Giving 4,000 skin test doses once a week three times will probably give a much better immunity, especially in young children. The older the individual, the more is required to produce immunity. Whether or not we can prove eventually that we have a permanent immunity, we have here a big contribution. If we are able to produce immunity for only one year, that alone is a big contribution. Producing a permanent immunity is, of course, the end in view.

DR. LARSON: I have often been asked by physicians what course to pursue in regard to administering antitoxin prophylactically when a number of members of a family have been exposed to diphtheria.

In general, I am opposed to the idea of giving antitoxin of any kind prophylactically. I would, of course, make certain exceptions to this rule. It is very unfortunate to sensitize a child to horse serum for reasons which are well known to all.

The work which Dr. Colby and I have been doing with scarlet fever, indicates that by giving the large doses made possible by injecting the toxin with the sodium ricinoleate, immunity may be established as early as four days following the inoculation.

Immunization against diphtheria requires a much longer time, for which reason it is impossible to combat an existing epidemic by active immunization.

DR. PLATOU: The use of the detoxified preparation of Dr. Larson certainly gives us, according to test, a rapid immunity without the usual hazards of anaphylaxis. The efficacy of the preparation will, of course, be determined by

further study and I certainly feel that Dr. Colby's work is a valuable contribution. In my own cases Dr. Zingher's toxin has been employed, and although I have been able to produce immunity which apparently stands the test of intimate exposure to the disease, yet the immunity does not appear in nearly so short a time. Some of my patients have apparently lost their immunity after a period of three or four months. Regardless of the interpretation of all these facts, it is safe to say that scarlet fever immunity can be accomplished and that the degree and duration of the same will depend on dosage, intervals between inoculations and types of preparations.

DR. SCHLUTZ: I have nothing to add at all. I really think we should be justly proud of the results, the fine contribution Dr. Larson has given the profession and the splendid way in which Dr. Colby has worked out clinical details.

DR. ANDERSON: I feel as Dr. Schlutz does, that we should be proud of Dr. Larson's contribution.

I wonder whether something could be done in the way of forming a committee concerning this subject. About two or three years ago when toxin-antitoxin was first used, Dr. Rodda suggested that we get together on the thing and determine the procedure that would be to the best advantage of the child. A plan was formulated and followed which, I think, has worked out satisfactorily for all concerned.

I wonder whether it would be possible for a committee to be appointed to see whether some such uniform plan of procedure cannot be assembled, so that the group will work together as one. I think it would be a good thing that the men all pull together instead of one doing one thing and one another.

DR. SCHLUTZ: At the request and suggestion of Dr. Pearce, the Department of Pediatrics of the University of Minnesota is now sending out a circular letter to all the pediatricians in this country, asking them to state their experience with the antitoxin and with the Dick test in scarlet fever. These letters are being sent to all the pediatricians and pediatric organizations and will, when returned, form the body of a very interesting report which will throw light on this problem. Of course, all the pediatricians will not have the advantage of comparing results such as are obtained here with Larson's modification of the test with those obtained by the Dick technic or by the New York Board of Health technic, but any general report should be very valuable. When the letters come in, a further report can be given.

DR. STEWART: I had seven cases of scarlet fever in which serum was given, one recent case in which the child had previously been sensitized to horse serum by diphtheria immunization. In this case the temperature rose to 104 F. on the second day, and the child had vomiting attacks every half hour for twelve hours. The child was very ill. In four other cases in which the Dochez serum was given there were severe reactions.

It is a great advantage when we can produce immunity to both diphtheria and scarlet fever without sensitizing patients to horse serum.

DR. BIRNBERG: I have had no experience with scarlet fever toxin, but wish to make a few remarks in regard to the toxin situation in Paris. They are no longer using toxin antitoxin mixtures in active immunization. Apparently France has become standardized on the active immunization treatment in diphtheria. They are using anatoxin, which is furnished free of charge by the Pasteur Institution of Paris. This is given in from 2 to 3 doses at two-week intervals. The advantages of anatoxin is that the immunization is more

rapidly obtained, apparently lasts longer and, most important, forces freedom of danger from sensitization to horse serum.

We now in St. Paul are using anatoxin, but are unable to give a definite report, due to the short length of time we have used it.

DR. COLBY: Last April, May and June, I performed a small series of extinction tests, using the different scarlet fever antitoxins on the market. At that time most of them were required to have at least an antitoxic value of 1,000 skin test doses per cubic centimeter. Most of them were concentrated five and ten times. Parke, Davis at that time had one of a concentration of 25,000 per cubic centimeter. That gave a very much larger extinction test, and one could get an extinction test using that antitoxin about thirty-six hours longer after the disease had commenced than with any of the other antitoxins. I think if we are going to use any serum at all, we should use the concentrated because it is more effective, as shown by the extinction test.

The adults to whom I gave the scarlet fever antitoxin at height of the disease said they were relieved of their aches and pains and headache and felt very much better in forty-eight hours, and we could see the disappearance of the rash after six or seven hours. I am convinced that if we are going to use scarlet fever antitoxin, we should by all means use the concentrated type.

INJURY FROM A FALL. Presented by DR. F. C. RODDA.

I believe it is our experience that we are seeing more and more cases of deaths and injuries from violence and accidents. In this connection, I wish to report a case of injury from a fall.

The case is that of a boy, A. W., aged 11 years, who fell from a scaffold and injured his side. The fall was not a great one. The scaffold was erected a short distance from the wall of the building at the level of the first story windows. The boy jumped out of a window and slipped down between the scaffold and the wall. He caught the scaffold with his hands and hung on, so that his feet were not more than a foot from the ground. He dropped from the scaffold and walked home.

I was called about 7 o'clock that evening. The boy was suffering from severe pain in the abdomen for which he begged relief. The only evidences of external injury were a slight abrasion over the left side of the chest and a cut of ½ inch long over the right side of the scalp. There had been no bleeding from any point whatever. The boy was in a state of shock, pale, with a rapid pulse and extreme rigidity of the left rectus muscle. We made a tentative diagnosis of some intra-abdominal injury. A surgeon was called who concurred in the diagnosis, and the boy was taken at once to the hospital. On admission, the hemoglobin was found to be 60 per cent.; the red cell count was 2,780,000 and the coagulation and bleeding times were normal. The patient did not void urine. Catheterization yielded a small amount of blood stained urine.

The question arose as to whether to enter the abdomen or not, but it was decided to do so. Dr. Stephen Baxter opened the abdomen. There was no evidence of hemorrhage or escape of fecal material. The bladder appeared to be intact. In the left upper quadrant, there was a large mass bulging forward, dark colored, evidently blood. This was behind the peritoneum. There was severe edema of the mesentery. It was very evident then that we were dealing with some kidney injury. The tumor projecting against the peritoneum explained the complaint of intense pain in the abdomen and rigidity of the rectus muscle. The abdominal wound was closed at once and an incision was made over the

left kidney region. When the kidney was exposed, the lower third was found to be completely fractured off from the rest of the kidney. (The specimen was passed around for inspection). The hemorrhage was nicely controlled and the wound was packed and closed.

For the first forty-eight hours, the boy passed a large amount of bloody urine. Since that time the urine has been clear. His temperature ranged from 100 to 100.5 F. He seemed to be making a good recovery.

It appears, from the literature, with an injury of this character that it has been the custom to remove the entire kidney. That would have been done in this case had it been feasible. The boy, however, was in a state of severe shock and we felt that, so far as the hemorrhage was controlled, his prospects were better to close the wound. If necessary, the kidney could be removed later.

I report this case to show a profound effect from a very slight injury. The opposite often occurs. We recently had a child who fell 20 feet, striking his head on a cement floor in a basement. Outside of a cut on the soft part over the right eye, there apparently were no other injuries.

This case also presents the question of whether one should go into the abdomen or not. It appears, in this case, that it was not necessary. However, if we had it to do over again in a case presenting similar symptoms, we would feel that an inspection of the abdomen, to rule out the rupture of a viscus, would be indicated. Apparently this patient suffered no ill effect from inspection of the abdomen.

DISCUSSION

DR. ROWE: Dr. Rodda has described a serious injury following an apparently trivial fall. The symptoms followed closely on the injury. It is to be remembered that the symptoms due to hemorrhage, either of the brain or of abdomen, may be delayed and may even be intermittent unless properly treated.

The child recently seen illustrated the latter type of case. Following an automobile injury accompanied by slight shock, the child was placed in the hospital for observation. At the end of two days he was discharged, apparently well. He was allowed to run about for a day, when severe pain and evidence of internal hemorrhage developed. He was again returned to the hospital, where the symptoms promptly subsided on rest in bed. After several days he was again discharged and again allowed to resume the normal activities of a child of 6 years. The symptoms again developed and he was brought to Duluth, where a diagnosis of fracture of the liver was made and proper treatment given. The recovery was rapid and permanent.

POLYARTHRITIS IN A SIX-DAY OLD INFANT ASSOCIATED WITH ACUTE RHEUMATIC FEVER IN THE MOTHER. Presented by DR. L. F. RICHDORF and DR. W. H. GRIFFITH.

Paper to be published in full in a later issue.

REPORT OF HIS RECENT TRIP TO EUROPE. AN INFORMAL TALK. Presented by DR. E. D. ANDERSON.

CHICAGO PEDIATRIC SOCIETY

Regular Meeting, Oct. 20, 1925

GEORGE E. BAXTER, M.D., *in the Chair*

ENDOSCOPY IN CHILDREN. (ILLUSTRATED BY SLIDES.) Presented by DR. EDWIN MCGINNIS (by invitation).

The first bronchoscopic work I ever saw was in 1909, when I started to assist Dr. E. Fletcher Ingals. He was the first, I think, who ever removed a foreign body from the tracheobronchial tree in this country, either he or Dr. Coolidge. Dr. Ingals' first case was that of a piece of a clay pipe that had become lodged in the trachea, and this was quite difficult to remove because the forceps at that time were not constructed so that they would hold on a slippery surface. These cases usually occurred in children and usually were neglected. I remember two patients, each of whom had aspirated a six or eight penny nail. This had lodged in the bronchus and in the first case had been in place for eight years. There was a large abscess in the right bronchus. Within two or three weeks we saw the second patient with the same condition in the left bronchus, with much destruction of tissue and the nail down in the lower part of the abscess. In passing the tube there was a fistula and a great deal of purulent material would be coughed into the bronchoscope, so it was very difficult to get near the foreign body. Both Dr. Ingals and Dr. Jackson had had forceps constructed with a curve, so that one could get hold of the nail or other foreign body.

The cases were not numerous at that time, and we had not thought of using the roentgen-ray and fluoroscopic screen as aids to the removal of these foreign bodies.

Recently, a woman told me I had saved her daughter's life three years ago. This patient was aged 27, and came to Dr. Anderson because a chicken bone had lodged in her throat. She had vomited and passed some blood in the stool. The roentgen-ray examination was negative but the bone was in the upper part of the esophagus.

In our first experience with foreign bodies in the esophagus we did not use the esophagoscope to get a direct view. The procedure at that time was to use a bristle probang, which as it passed down would slide through, and by manipulating the handle the bristles would be released after the instrument had passed the foreign body, the idea being that as it was pulled out the foreign body would be caught in the bristles and removed. There are many instances in which the foreign body has been pushed down into the esophagus by the physician who first saw the patient. This is a dangerous procedure, because in blind pushing one cannot tell how much damage will be done.

The work is divided into three parts, the diagnosis, treatment and removal of the foreign body. The dramatic part of the work is the finding and removal of foreign bodies from the esophagus, larynx or air passages, and with the esophagoscope one can also diagnose strictures and ulcers of the esophagus. A case referred by Dr. McNeal last summer was that of a new-born child who, after nursing, regurgitated the milk. There was evidently no opening from the esophagus to the stomach, but with the esophagoscope I was able to find a little pouch and a small channel connecting with the trachea and the bronchus. I have had one or two cases of spasmodic esophagitis, in which I could see definitely ulcerated areas in the esophagus.

In the treatment of patients with esophagus trouble, the nicest part of the work is in the treatment of strictures following the swallowing of lye. The late Dr. Sippy helped many of these patients by having them swallow a string and then using olivary dilatation over a wire. With the esophagoscope, a fine filiform bougie can be passed by sight; then by connecting it with the electric current one can raise the heat to 45 C., which proves very effective in many instances. One can pass a No. 12 bougie, heat it to 45 C., keep this in place for twelve minutes, and then pass a larger olivary through the stricture. If one attempts to push such a bougie through without the heating, it tears and damages the parts.

There are two or three tracheal conditions that can be helped. If there is a good deal of fluid, with gurgling râles and a cough, one can pass a fine aspirating instrument into the bronchial tree and aspirate as much fluid in two or three minutes as a child can cough out in two days. The Bronchoscopic Clinic in Philadelphia has been doing some work on the bronchoscopic treatment of asthma.

Perhaps the best part of the work has been the bacteriologic part. The fluid has been aspirated under aseptic conditions, certain bacteria have been found, namely, *Streptococcus viridans* and in some instances *Streptococcus hemolyticus* and *Staphylococcus aureus hemolyticus.* Ciliated columnar cells that were exfoliated have also been examined. I have wondered whether these bacteria pass down through the bronchi and trachea, or whether they pass through the lymph channels, get into the lungs and then produce a round cell infiltration that causes exfoliation of the bronchial mucous membrane cells. One fact of interest about the ciliated columnar cells was that they could be kept alive under salt, and the cilia could be seen in motion. As high as from 300 to 360 cilia have been counted to each cell. They have two types of wave motion, one the flagellated and the other starting upward. In the lung abscess cases a few of the degenerated columnar cells have been obtained, but they were not alive and the cilia were entirely destroyed.

If areas of granulation tissue are present in the bronchus and a tube is passed, the granulation tissue may be scraped away or treated with silver nitrate to destroy the granulation. Otherwise, these granulations become so large that they constrict the bronchus and cause retention of the fluid. Jackson has cauterized this granulation tissue and reestablished the lumen of the bronchus. Bronchoscopy is indicated in cases of abscess. My first case of this type was that of a woman, aged 42, who had the tonsils removed, under general anesthesia, by a surgeon who used the Sluder operation. The anesthetist was one of the best in town. There was considerable hemorrhage following the tonsillectomy, and the patient had to be kept under the anesthetic for quite a while until the pillars on both sides were sutured together. There was considerable purulent content in both tonsils. Three days later, there was a rise in temperature, accompanied by cough and pain on the left side. The temperature was elevated only 1 degree and the patient was sent home in three days. She returned to the hospital three weeks later with an increased temperature, pain in the left side and unproductive cough, accompanied by great depression. She had been seen by several internists, and I was asked to see the patient about six weeks after tonsillectomy. I passed a bronchoscopic tube, and as it passed the trachea I got the typical lung abscess odor. The trachea and bronchi were all dry. In passing the tube into the left bronchus, the tube met an obstruction and on inspection I saw what looked like a clot of blood. We decided that some blood had slipped down into the bronchus during the

operation, had become coagulated and had shut off the air going into the bronchus. There was no air going into the left lower lobe. I aspirated and broke up the clot, and soon afterward the patient had a productive cough. We used the bronchoscope several times, with arsphenamin intravenously and the patient got along well, but the surgeons in the case finally performed a rib resection and went in from the outside. The point of interest was that when the surgeon put his finger into the resection wound, something popped up into the trachea which proved to be a blood clot. No cavity was found, but a drainage tube was put into the lung and the surgeons felt that external operation was of great value.

In the cases at the Children's Hospital, there was the typical saprophytic secretion; I think it is always well to get air into the bronchus for its helps to eradicate or to arrest the saprophytic growth.

In the removal of foreign bodies the most common objects are coins and telephone slugs. (Lantern slides.)

In the endoscopic work in the foreign body and bronchial cases there is nearly always infection, and the operator should protect himself well to prevent the development of upper respiratory infection. He must wear a gauze mask and glasses.

In some of the patients with coins in the upper end of the esophagus, the condition looks simple, but unless one has proper instruments and some experience, he is likely to have much difficulty in their removal.

DISCUSSION

QUESTION: In the cases in which the child has swallowed a peanut, how long is it before the infiltration is sufficient to show in the roentgen-ray plate?

DR. MCGINNIS: About thirty-six hours. In one case a grain of corn had lodged in the left bronchus and caused complete blocking. In the afternoon a complete shadow was revealed on that side. The complete blocking of the bronchus caused collapse and the heart, lung, mediastinum and everything was pushed over to the left side. The attending physician thought the child had pneumonia and should not be operated on, but I told him I thought that with removal of the plug the lung condition would clear up, as it did in the patient I showed you on the screen; my prognosis proved to be correct. If half a peanut is swallowed, it will block up the bronchi and cause the same effect. If fine particles of peanuts are caught in the bronchi, Jackson says there is a substance in the peanut that causes the irritation. Mosher takes exception to this, and considers the irritation due to retained secretion from the plugging up of the small bronchioles. There is always a lot of secretion in the blocked area and in such cases the bronchi must be aspirated very quickly to prevent the patients from drowning themselves.

Whenever a child is brought in with a definite history of a choking spell, he should always be examined with a bronchoscope. Two or three months ago, I had occasion to note this very definitely. A child, aged 3, got some peanuts into his mouth, had an inspiratory effort and cough, some cyanosis and a little wheezing for two or three hours, and then the condition apparently cleared up. A few days later, the child developed a rise in temperature and cough, and the family physician was called. He was told of the choking episode but made light of it, and said he was sure the child had bronchial asthma. He treated the child for two weeks but with no improvement, and he asked for consultation. The physican who was called had read one of my

articles, and thought of foreign body when he listened to the chest sounds. I was called into consultation, and we removed the peanut.

DR. JOSEPH BRENNEMAN: I wish Dr. McGinnis would say a little more about abscesses. It is not clear in my mind at just what stage the bronchoscopist can do anything for these patients. Is this procedure most effective when the child is coughing up pus, or can you open the abscess in that way and drain it into the bronchi? It seems to me there is a distinct field of usefulness, but I do not quite understand just where it is.

DR. MCGINNIS: I do not think the so-called abscesses that follow tonsillectomies are real abscesses. I have examined four patients at the Presbyterian Hospital, and last May, Dr. John A. Cavanaugh reported a case of a lung abscess following the removal of a safety pin in the lower part of the esophagus. His patient had had two anesthetics and developed a lower lobe abscess. In the literature this condition is usually in the lower lobe. The infection follows down, just as the foreign body follows, into the lower main bronchus. The four patients at the Presbyterian Hospital were treated surgically, and a needle puncture was used in the attempts to aspirate. Only a little drop of pus was obtained after several attempts. I think the operators got into a fine air cell and simply aspirated that air cell. In the abscesses following tonsillectomies I think the cheesy material is squeezed out of the tonsil, and is inspirated into the bronchus, some blood follows down and seals it off. Then the saprophytes begin to grow and attack the mucous membrane. If we can get the patients early and dislodge the clot, I think we can do the most good.

In the patient with three abscesses at the Children's Hospital, there were some blood clots in the bronchi. In the literature, the consensus of opinion is that these are conditions for aspiration. I do not think the type of material that is found in them could be carried around hematogenously.

DR. BRENNEMAN: One of the cases at the Children's Hospital was unusually interesting. Following tonsillectomy, the child apparently had three abscesses, one above and one below on one side and one on the other side. The one on the left increased to three or four times its original size in a few days. Dr. McGinnis did the endoscopy, and the child developed pneumothorax on the side of the two abscesses. The temperature went down, and some very offensive material was coughed up for a day or two. The temperature has returned to normal and the child is well. I agree with Dr. McGinnis that these are not real abscesses. This entire condition has cleared up, in a short time, which I have never seen happen except in this case.

DR. ARTHUR H. PARMELEE: I was hoping something would be said about the heated bougie in these cases. This came to my attention because one of the patients treated by Dr. McGinnis had been at St. Luke's Hospital for about two years. The child had swallowed some lye and had almost complete stricture of the esophagus. After being on liquid diet for some time, Dr. Halstead performed a gastrostomy and inserted a tube, by which the boy was fed for some time. He did fairly well, but we were fearful that he would get some solid food, which always caused dehydration for several days and much difficulty. We finally sent him over to the Children's Hospital for treatment by Dr. McGinnis, and by means of the heated bougie the stricture has been almost entirely healed. The gastrostomy wound has been permitted to heal up, and the child is doing well in every way and eating everything he wishes.

Dr. Jesse R. Gerstley: The following case may be of interest in connection with this discussion. A child had been having difficulty in swallowing, with associated pain behind the sternum for some time. The roentgen-ray examination showed a smooth, rounded narrowing of the esophagus in an area the size of a hazelnut, somewhat above the stomach. The child gradually became worse, and a gastro-enterologist was called in. He decided to use the esophagoscope. When he reached the area in which the pain was complained of, he felt a very slight obstruction, which immediately melted away, and on looking in, a somewhat reddened, very small area on the posterior wall of the esophagus was found. On withdrawal of the tube, the child experienced excruciating pain and almost fainted. On recovery she was taken home but that evening the pain continued. I saw her for the first time the following day. She then presented the picture of severe empyema and was almost moribund. The physical findings were typical of empyema and the aspirating needle showed large quantities of purulent fluid. The child died within a few hours, and postmortem examination showed a fibrous walled tumor, the size of a hazelnut, on the posterior wall of the esophagus. The wall of the esophagus was intact, but the pressure of the esophagoscope through the wall had ruptured the tumor. The purulent contents had then discharged into the pleura.

Dr. George E. Baxter: I wish to emphasize what Dr. McGinnis said about paying attention to the history of the swallowing of a foreign body. In one patient I saw in consultation, the child had been treated for laryngeal diphtheria, had received the usual amount of antitoxin but had made no progress. There was a very clear history of the swallowing of a chicken bone, but the attending physician had not attached any importance to that and thereby had overlooked the real cause of the trouble. We made a diagnosis of suspected foreign body, in the absence of Dr. McGinnis, and the patient was taken to Dr. Boot, who removed the bone. In another patient with a history of swallowing a foreign body, the interns did not pay any attention to the history, but a foreign body was subsequently discovered by roentgen-ray examination. We should always be on the lookout for these cases, and not ignore the history.

Book Reviews

FEEDING AND THE NUTRITIONAL DISORDERS IN INFANCY AND CHILDHOOD. By JULIUS H. HESS, M.D., Professor and Head of the Department of Pediatrics, University of Illinois College of Medicine; Chief of Pediatric Staff, Cook County Hospital; Attending Pediatrician to Michael Reese and Englewood Hospitals; Consulting Pediatrician, Municipal Contagious Hospital, Chicago; Member of Advisory Board, Children's Bureau, Department of Labor, Washington, D. C. Fourth Revised and Enlarged Edition. Price, $4.50. Philadelphia, F. A. Davis Company, 1925.

The practical aspects of this book are especially to be commended. Dr. Hess has presented the technic of infant feeding in a sane and conservative way, entirely consistent with the best practices of the present time. To the student and general practitioner this book should serve as a useful guide to proper infant feeding.

It is unfortunate that the treatment of the physiology of nutrition cannot be equally commended. It would be, of course, impossible adequately to give a complete presentation of this subject in a small book. As a result, this section abounds in half-truths which may be misleading. Brevity has led to dogmatic statements which are based on observations of not fully established accuracy, and consequently may give erroneous impressions to the uninformed reader. For example, the tolerance of infants to different sugars is compared, without intimation that the subject is still unsettled and that the methods by which some of this information was derived are open to considerable question. The description of fat digestion can only give a very hazy idea of the present conception of its mechanism. The great number of such defects would make it seem advisable to rewrite the section on physiology so as to present the subject adequately, or if space does not permit this, it should be omitted altogether.

The weakness of the portion of the book dealing with physiology is in marked contrast to the other sections. The nutritional disorders are well described in a manner which is clear and sufficiently comprehensive. Occasional errors and obscurities are evident, but they are insignificant and will unquestionably be eliminated in future editions. The preparation of this book by Dr. Hess represents a real service, and in this enlarged and revised edition it should find a considerable demand.

OPENING DOORS. By JOHN THOMPSON, M.D., F.R.C.P. (Edinburgh). Edinburgh and London: Oliver and Boyd, 1924. Purchasable in U. S. A. from American Child Health Association, 370 Seventh Avenue, New York City. Price, 10c.

The mentally defective baby has not fared well at the hands of the physician. It is no easy task to determine the mental status of a baby. When we do satisfy ourselves that he does not measure up to the normal, we are perplexed as to the kind of advice to give the mother and how to present it.

John Thompson, F.R.C.P. (Edinburgh), the distinguished Scottish pediatrician, who has contributed so liberally and effectively to the literature of pediatrics, has prepared a pamphlet which every pediatrician should read. It is entitled "Opening Doors" and is addressed to "Mothers of babies who are long in learning to behave like other children of their age." It is a unique

contribution, coming out of his many years of experience. It tells the mother how the normal baby should develop, how to determine "when the baby's brain is not growing as fast as usual," and then points out to her in clear, concise language the contribution she can make toward the infant's development. Never once does he suggest to her that her baby is feebleminded, and always holds out to her hope for the success of her efforts. The document has a high psychologic value. It is intensely human and it should point out to everyone who reads it the importance and necessity of recognizing these cases, the value of rightly directed supervision and the desirability of withholding from the mother the fact that her infant is feebleminded, but humanely directing her in the carrying out of a program which does offer hope of reward.

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